Medico-legal report

Adam Strain

Dob: 4th August 1991
Dod: 28th November 1995

Prepared on behalf of:

THE INQUIRY INTO HYPONATRAEMIA RELATED DEATHS
Chairman Mr John O'Hara QC

By:

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I am Dr Waney Squier, Consultant Neuropathologist to the Oxford Radcliffe Hospitals and Honorary Clinical lecturer in the University of Oxford. I have been a consultant neuropathologist since 1984 having trained at the Institute of Psychiatry and Great Ormond Street Hospital for Sick Children. During my 27 years in Oxford I have specialised in the pathology of the developing brain in the fetus and neonate. My other areas of interest are developmental causes of epilepsy and muscle pathology. I have been involved in research into the nature and timing of brain damage due to intrauterine and perinatal insults, the effects of asphyxia on the immature brain, correlation of imaging and anatomic pathology in the pre-term human brain and the neuropathology of cerebral palsy in children. I have published widely on these subjects in peer reviewed journals and have edited a book "Acquired Damage to the Developing Brain: Timing and Causation". I am a member of the British Neuropathological Society and the British Paediatric Neurology Association. I am a fellow of the Royal College of Physicians,(by election following membership by examination in paediatrics) and a fellow of the Royal College of Pathologists.

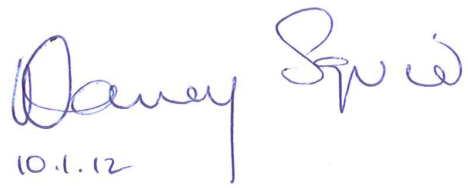
In the last ten years my experience with infant brain pathology has extended to many forensic cases and I have written reports and given evidence in court for both the prosecution and the defence in many cases of sudden unexpected death in infants.

My expertise is based on my experience in examination of the brain, spinal cord and dura after death and as such assists in the interpretation of the mechanisms of injury and the imaging of the brain.

I understand that my overriding duty is to the court in preparing reports and in presenting evidence. In preparing this report I have attempted to provide an unbiased analysis of the facts of this case from the perspective of the neuropathology and based on the current state of scientific knowledge, the current peer reviewed literature and my personal professional experience.

I have attempted to be as accurate and as complete as possible and my opinions are restricted only to those subjects which are within my area of expertise. I believe that the facts I have stated in this report are true and that the opinions I have expressed are correct.

Dr Waney Squier MBCHB FRCP FRCPath



Consultant Neuropathologist

Honorary Clinical Lecturer

In preparing this report I have examined sections of brain tissue from 18 wax blocks labelled Strain F46728; they have been stained in my Departmental laboratory in Oxford.

I have been sent the documents as set out in Appendix 1 and have reviewed those which are relevant to my expertise. I have not seen the original autopsy or neuropathological report. I have not seen any post-operative brain scans or their reports. I have not seen the deposition of Dr Armour.

The background to this boy's illness and death are set out in the brief. Essentially Adam Strain was born with renal abnormalities. He was clearly unwell in his first year of life and required fundoplication to prevent gastro-oesophageal reflux. His renal problems were severe and he required a renal transplant. He was offered a kidney in November 1995 and surgery took place on 27.11.95. Anaesthesia was induced at 0655. His pre-operative neurological condition is not described and I assume that there were no concerns prior to anaesthesia. At 1155, five hours later after surgery was complete, Adam failed to wake from anaesthesia and his pupils are described as fixed and dilated. He was transferred to PICU for ventilation. 7 ½ hours later (at 1935) brainstem testing was carried out and repeated at 9.10 am on 28.11.95. Ventilatory support was withdrawn at 1130 on 28.11.95, almost 24 hours after surgery was finished. An autopsy was performed on 29.11.95 by Dr Armour and the brain was examined by Dr Mirakhur.

Neuropathological Findings:

(The detailed microscopic findings are set out as a technical report in appendix 2.)

Summary of Neuropathological Findings:

The appearances are of a normally formed brain with moderate oedema. Many cells are swollen and vacuolated and there is vacuolation of white matter, most marked around blood vessels and in the deep cortex.

There are a small number of nerve cells undergoing early necrosis; these are most marked in the subventricular cranial nerve nuclei of the pons.

There is no evidence of marked tissue compression or parenchymal or subarachnoid bleeding in the medulla or hippocampus.

Special stains show no activation of microglial cells and few cells show early necrosis. Aquaporin expression shows a few swollen astrocytes, which are also identified with GFAP. There is no glial activation. ßAPP shows widespread expression in axons, some swollen, in the white matter. This change is typical of metabolic axonal disruption and is most commonly seen in hypoxic / ischaemic injury.

There is no evidence of meningeal or parenchymal infection, no meningitis or encephalitis. There is no evidence of trauma or other acquired disease. There is no evidence of malformation or of old acquired brain damage.

Comment

Brain swelling

Brain swelling is assessed by several criteria. These include the pre-mortem brain scan appearances, brain weight, naked eye appearances of the brain before and after fixation and slicing and histological appearances.

CT or MRI imaging

I have not seen scan images or reports.

Brain weight

Hausmann (Hausmann, Vogel et al. 2006) concluded that fresh brain weight, compared with standard tables for expected weight for age, is the most reliable criterion for grading brain swelling. Standard weight charts must be used with caution as fresh weights are usual in American standards and fixed in European (Guihard-Costa, Menez et al. 2002). Two charts consulted indicate that the expected fresh brain weight for a boy of 4 years is between 1290g (when expected body weight is 17.5kg (Keeling 2009) and 1310 g (expected body weight of 19.46kg (Dekaban 1978). Adam's fresh brain weight is within normal limits.

The recorded fixed brain weight of 1680g is 118 % of the expected weight. (The standard expected weights cited above, with 10% added for formalin fixation, are between 1419 and 1441g.) Even if this weight is correct, it does not represent massive brain swelling. My experience with this age is limited. In a recent study of much younger brains (which may have greater potential for swelling) the weights ranged from 103 to 158% of the expected weight.

Macroscopic evaluation

Brain swelling is manifest by effacement of the sulci[1], by herniation[2] and by compression of the ventricles[3]. Macroscopic assessment is best made at autopsy or during initial neuropathological examination of the fixed brain. I do not have the reports of the autopsy or of Dr Mirakhur's neuropathology report.

I note that Dr Armour published this case in 1997 and included two photographs. These are not of good quality but they do not indicate that swelling is extremely severe; the cortical sulci are not fully effaced and the ventricles, although narrowed, remain patent. I am concerned at the use of the fixed brain weight in this report as this may be artefactual. This is further discussed below.

Microscopic evaluation

Microscopic features of brain swelling include increased perivascular spaces and vacuolation, particularly of the white matter. The brain swelling seen histologically in Adam's brain is moderate and not as severe as a number of cases in my experience. It is difficult to be certain of the degree of swelling on the basis of histology as vacuolation of tissues is easily induced by artefacts such as

[1] The spaces between the normal folds of the brain surface
[2] In herniation brain swelling forces parts of the brain out of their normal confines. The two most common sites of herniation are the parahippocampal regions in the medial temporal lobes and the cerebellar tonsils, where herniation leads to compression of the lower brainstem at the cranio-cervical junction.
[3] The normal fluid containing cavities within the brain.

delayed or suboptimal fixation. Further, it has been shown that histological assessment of oedema does not correlate with other markers of swelling or the chemical estimation of brain water (Haussmann 2006).

I have used an additional criterion, aquaporin expression, which is not well studied but I have used it in studies in progress of the brains of younger infants. Aquaporins are water channels found within cell membranes and show upregulation in severe brain swelling (Wright 2010). There was only moderately increased aquaporin expression in this brain.

Hypoxic-ischaemic Injury (HII)

There is no significant pathology to indicate HII in this brain. Only a few cells in the dorsal pons show early neuronal death. There is no microglial activation and no blood vessel change. Patients with brain swelling who are nursed on a ventilator may show reduced cellular reactions as the blood supply to the tissues is impaired. Despite this, had there been significant HII I would have expected to see some reactive changes considering the child survived for 24 hours after failing to wake following surgery.

Axonal damage

Many groups of swollen axons in the white matter expressed βAPP. This is commonly seen in HII but is also described in other metabolic disruptions. It has been described in hypoglycaemia (Dolinak 2000) and in electrolyte disturbances such as hyperkalaemia and hypernatraemia (Reichard 2003).

I am not aware that it has been described in hyponatraemia but this may be the explanation in this case in view of the lack of evidence of HII.

Osmotic myelinolysis

One of the best known neuropathological associations of hyponatraemia is focal myelinolysis, commonly, but not exclusively, found in the pons. I have stained a number of brain areas with a myelin stain and have seen no evidence of myelinolysis. This condition is thought to be related to the speed of correction of hyponatraemia.

Conclusion

The brain is moderately swollen but its cause is not determined. There is no evidence of HII or of any other pathological process. There is no evidence of osmotic myelinolysis. There is nothing in the histology of the brain which explains Adam's failure to wake after surgery.

Requirements

In responding to your specific questions I have inserted my responses beneath each question. To assist with my responses to a number of these questions I have reviewed available information from cases of 4 year olds whose brains have been examined in this department. There are not many; readily available records as far back as 1970 revealed 10 cases. This cannot be regarded as anything more than a rough guide as the sample is small and a detailed analysis of the cases was not made due to time constraints. The detailed pathology has not been taken into account, although two cases

with pathology relevant to brain weight are identified. Cases are both male and female and body weights were not included. The information is presented in Table 1.

34. The Inquiry team requires your assistance with the following matters, arising out of the material received to date and the guidance of the Inquiry's Expert Advisors:

(1) Given Adam's age and his weight of 20.2kg, is 1,302gm or 1,320gm a reasonable figure for the pre-operative (dry) weight of Adam's brain? What is the possible range of Adam's pre-operative dry brain weight?

There seems to be some confusion over the weight of the fresh brain, although the weights cited are not significantly different. I have based my calculations on a median of 1310g. (I assume the term pre-operative dry brain weight refers to the expected weight of the fresh, unfixed brain as noted at autopsy). As noted above, the average weight for a male of 4 years is between 1290 and 1310g.

(2) What effect (if any) does the process of 'fixation' have on brain weight?

Fixation leads to a slight increase in the brain weight (Guihard-Costa, Menez et al. 2002) (Ravid and Swaab 1993); the rule of thumb in daily practice is about 10-12%. In my departmental series there was a considerable range of increases in weight with fixation from 1-15%. Adam's brain increased by 28%- almost twice that of any case in this small series. This, together with the fact that the fresh brain weight was correct for his age, suggests that the fixed brain weight was inaccurate.

(3) What is your experience or knowledge of a child of 4 years and weighing 20.2kg having a post-mortem fixed brain weight of 1,680gm?

This is an extremely heavy brain for a 4 year old child based on standard tables. My experience is limited as fortunately few 4 year olds die and have brain examinations. Table 1 shows that Adam's fresh brain weight is within the observed range, the fixed brain weight is more than any except case 1 which was noted to be abnormally large and had a tumour.

(4) What (if any) is the significance of the weight of Adam's cerebellum having been recorded at 154gm and his brain stem at 22gm?

The hindbrain (brainstem+ cerebellum) usually weighs about 12% of the whole brain weight in the adult. In neonates the cerebellum is proportionally much smaller as it is still actively growing at this time (Roessmann 1974). However, I regard these weights as unreliable. The point at which the hindbrain is removed from the brain and the length of the lower brainstem retained at its junction with the spinal cord may vary considerably. In Adam's case the hindbrain weighs 10.5% of the whole brain. It is a little lower than the range in the departmental series, but the images in the case report (Armour 1997) indicate that the brainstem was cut high with a short segment of upper cervical spinal cord, which would reduce the weight of the hindbrain. I do not think these weights can be regarded as significant.

(5) Dr. Armour weighed Adam's brain on 29th November 1995 (therefore pre-fixation) and appears to record in her notes a weight of 1,302gm corrected to 1,320g. She also records in her

description of organs after fixation that Adam's fixed brain weight was 1,680gm. What is the likely reason for the difference between the pre-fixation and fixed brain weights?

Some weight gain would be expected due to fixation. In this case the increase is large, 28% which suggests that there has been an inaccuracy due to different scales, uncalibrated scales or human error. My evaluation of the brain swelling from several aspects (see above) suggests that the fresh weight is more likely to be correct than the fixed weight.

(6) In your experience how likely is it that a post-mortem fixed brain weight is inaccurate, ie what are the likely chances of 1,680gm, which is recorded in the Report of Autopsy as the fixed weight of Adam's brain at post-mortem being inaccurate due to uncalibrated scales or human error?

I think it is likely that the fixed brain weight is inaccurate. The difference between the fresh and fixed weights of Adam's brain is twice that of any case from this department where the information is available. Published figures indicate that the expected increase due to fixation is 10-12%. In Adam's case the difference was 28%.

(7) What extra-cerebral fluid space is available in a 4 year old like Adam to allow 'reserve capacity' to accommodate cerebral oedema?

I am unable to give an accurate answer to this question.

There is some reserve capacity around the brain to compensate for swelling. However this reserve capacity varies between infants and adults and the relationship between increasing intracranial volume and intracranial pressure alters with age. Intracranial pressure rises very sharply after relatively small volume increases in infants; by the age of 14 this pressure curve is less sensitive (Leestma 2009) (pages 355-361). The response of the brain to increasing intracranial volume may not simply be due to mechanical and physical properties but is more likely to be related to immature anatomy and physiology.

(8) If Adam had any degree of cerebral oedema before surgery, what effect is that oedema likely to have on such a 'reserve capacity'

If there was oedema before surgery I would expect it to compromise any reserve capacity. While this is not my expertise, I would expect developing oedema would have been manifest in some way, even if subtle, for example abnormal behaviour or headache or sleepiness. He was admitted to hospital and observed by professionals for 11 hours, during which time clinical signs of oedema would be expected to be observed.

(9) If Adam's total body water was expanded by 10 per cent at 09:32 on 27th November 1995, what effect would that have had on his brain weight?

If there was osmotic overload I would expect the brain to swell.

(10) Is it possible to calculate what proportion of cerebral oedema can be accounted for by the volume of fluid given and the rapid fall in serum sodium?

I cannot answer this question. This is a very complex subject and not within my expertise.

(11) If Adam had suffered irrecoverable brain damage from oedema by some time between 09:32 and 11:30, is any continuing accumulation of oedema relevant?

If Adam had suffered brain damage due to oedema by 1130 the only relevance of continuing oedema would be the appearance of the brain on scans or at autopsy. Continuing brain swelling leads to flattening of the gyri, compression of the sulci and herniation, which would be apparent at autopsy.

The most dangerous effect of brain swelling is that, because the brain is contained within the closed box of the skull, it compresses the blood vessels leading to obstruction, first of venous outflow, then of arterial inflow to the brain tissue. Once this happens the brain tissue is deprived of its blood, oxygen and nutrient supply and the cells begin to die. Very little cell death was seen by histology.

(12) Is it possible to calculate how much oedema there was likely to have been at 09:00 and 11:30? If so, how could that be done? Is it possible to estimate what Adam's brain might have weighed at 09:32 (when his serum sodium was recorded at 123mmol/L) and at 11:30 (when his serum sodium was recorded at 119mmol/L)? If so what is your estimate of his brain weight at both of those times?

I do not think so.

(13) Describe and explain, to the best of your expertise, the likely progression or otherwise of cerebral oedema in a child who is being kept alive only by mechanical means. In particular:

(a) state if it was likely that Adam's cerebral oedema would have progressed further after 11.55 on 27th November 1995 when he was reported as failing to awaken from anaesthesia and having fixed dilated pupils

The oedema may well have progressed further as noted above (Q11).

(b) if so, how long and to what extent the cerebral oedema would have progressed thereafter. In particular, whether it would have progressed until ventilation was abandoned 22 hours later

It may have continued in which case the brain would have been likely to be visibly very swollen at autopsy. In many such cases herniation is so severe that cerebellar tonsillar material is displaced around the spinal cord. This was not seen.

(c) explain how relevant it was to his death given that timing of death depended not on a clinical event but on an artificial construct, namely the performance of brain stem death tests at 12 hourly intervals

The fact that the pupils were fixed and dilated and Adam failed to wake or breathe at 1155 immediately after surgery indicates that the vital functions were already impaired at this time. The brainstem death tests are indeed an artificial construct as life support could have been maintained indefinitely despite brainstem failure. I consider it more realistic to consider death to have effectively occurred prior to 1155am on 27.11.95, but this is a matter better dealt with by someone with clinical expertise.

(14) What effect (if any) could any impairment to Adam's cerebral blood flow whilst he was in the operating theatre have had to the level of his cerebral oedema when he left there? If it could have had an effect on it, then what contribution (if any) could that have made to his ultimate gross cerebral oedema, assuming that he was adequately oxygenated in PICU?

Impairment of blood flow damages brain tissue. This leads to brain swelling which may take 72 hours to reach a maximum. It would exacerbate any osmotic oedema due to dilutional hyponatraemia.

(15) State whether you believe there is any suggestion or possibility of Adam having cerebral tissue hypoxia, separate from anything caused by dilutional hyponatraemia itself:

There was very little evidence of hypoxic damage or indeed any cellular reactive change in the brain. The tissue changes begin within a few hours of hypoxic insult and are readily seen after 1-3 days. As these normal tissue reactive changes depend on influx of cells from the bloodstream they may be slowed or muted by failure of perfusion by fresh blood due to brain swelling. In this case I do not think this is an explanation as the tissue was well preserved. I do not think there was evidence of significant HII or of brain swelling of sufficient severity to compromise perfusion.

(a) If so, state whether it is possible that such hypoxia would have been sufficient to cause or materially contribute to the cerebral oedema which developed

Not in my opinion.

(b) Explain the role, if any, of anaemia in the pathogenesis of cerebral hypoxia and/or cerebral oedema

Anaemia will reduce the oxygen carrying capacity of the blood and may exacerbate the effects of hypoxia and oedema by increasing the mismatch between metabolic requirements of the brain and the fuel supplied.

(16) If Adam was anaemic at some stage (until correction by transfusion), then what effect (if any) could that have had on his cerebral oedema?

It may have exacerbated the effects of hypoxia and oedema.

(17) Can the use of dopamine contribute to cerebral oedema? If so, how and to what extent? Given the amount of dopamine prescribed for Adam and when it was administered to him, is it possible that it could have affected the extent of his cerebral oedema? If so, can you estimate the likely extent of its contribution in Adam's case?

I am aware that dopamine may exacerbate cerebral oedema in the experimental situation. However I do not have experience of the use of this drug clinically and this question if not within my expertise.

(18) Does the weight of Adam's brain at 1,680gm imply a cause of death other than dilutional hyponatraemia? If so, what might that be?

I think this brain weight is unreliable. The presence of brain swelling cannot determine its cause. It is a non specific and very common reaction of the brain to a variety of insults.

What is the likely contribution to that brain weight of:

- The dilutional hyponatraemia

I do not know

- Any cerebral tissue hypoxia between operation and death

There is no histological evidence of hypoxia; it would have to have occurred very shortly before death.

- Any anaemia Adam suffered during surgery and

I do not know.

- The dopamine that was administered

I do not know.

(19) The likely effect on the weight and appearance of Adam's brain of all that occurred between his coning in the operating theatre and the withdrawal of ventilatory support, including the process of coning itself as well as the fluids and medication administered to him over that period.

These events may have contributed to brain swelling. They may have reduced the cellular reactive processes so muting the changes seen microscopically.

35. To assist you we have attached an index of 'key documents' together with a file of the documents that would appear to be of especial significance. Please request any other documents that you consider relevant for the preparation of your Report

Dr Armour's report

Dr Mirakhur's report

Any postoperative brain scans and the reports.

W Squier

October 15th 2011

Appendix 1

INDEX OF KEY ACCOMPANYING DOCUMENTS

Tab.1 Brief

Tab.2 Selected Inquest Documents:

Depositions:

- Dr. Maurice Savage (Ref: 011-015-109)
- Dr. Alison Armour (Ref: 011-010-030)
- Dr. John Alexander (Ref: 011-012-079)
- Dr. Robert Taylor (Ref: 011-014-096)

Reports:

- Professor Peter Berry (Ref: 011-007-20)
- Dr. Edward Sumner (Ref: 011-011-042)

Tab.3 Selected PSNI Documents:

Reports:

- Professor Peter Berry (Ref: 093-030)
- Professor Risdon (Ref: 093-031)
- Medical opinion of Dr. Edward Sumner, including PSNI brief (Ref: 094-001-001 and Ref: 094-002-002)

Tab.4 Selected Inquiry Documents:

Initial Witness Statements of:

- Ms. Debra Slavin (1st)
- Dr. Maurice Savage (1st & 2nd)
- Mr. Patrick Keane (1st , 2nd & 3rd)
- Dr. Robert Taylor (1st & 2nd)
- Dr. Mary O'Connor (1st , 2nd & 3rd)
- Dr. Edward Sumner (1st)

Other Inquiry documents:

- Letter dated 2nd March 1995 from Dr. Maurice Savage to Adam's GP, Dr. Scott (Ref: 057-072-133)
- Autopsy Request Form
- Letter dated 10th May 2011 from State Pathologist's Office to the Inquiry attaching the contemporaneous notes of Dr. Alison Armour
- Adam's medical notes and records for 26th November 1995 – 29th November 1995

Appendix 2

Detailed Neuropathological Findings:

14 stained sections labelled STRAIN F46728 have been received for an opinion.

Two kidney samples each with 6 stains, one H & E stained kidney sample and trachea have been received. No brain tissue.

18 wax blocks of brain tissue have been received and sections stained in Oxford.

Spinal cord - 3 sections. The spinal cord is normally formed. The white matter contains many small vacuoles indicating fluid accumulation (oedema). The grey matter is intact, nerve cells appear normal. There is no displaced cerebellar tissue around the cord in these sections.

The medulla is normally formed. The white matter is finely vacuolated and fragmenting due to oedema. Nerve cells are intact.

Pons- (5 sections)The pons is normally formed but oedematous. Some scattered nerve cells are eosinophilic with dark nuclei lacking normal structure indicating early nucleolysis. These damaged cells are most frequent in the cranial nerve nuclei beneath the IVth ventricle. There is no evidence of infection or venous thrombosis. Blood vessels are intact and there is no haemorrhage or infarction in the tissues.

Midbrain - 1 section. The midbrain is normally formed and the aqueduct is patent.

Cerebellum - 2 sections. The cerebellum is normally formed and development consistent with age. There is some oedema which is particularly marked in the Purkinje cell layer. The dentate nucleus is normal. Cell necrosis is not seen.

Left cingulate; basal ganglia, hippocampus (3 sections). The tissue is normally formed but oedematous.

Right frontal, occipital, hippocampus (3 sections). The tissue is normally formed and oedematous. The hippocampus is a little less oedematous than elsewhere but the cortical neurones are shrunken and pyknotic. There is no perivascular haemorrhage.

SPECIAL STAINS

Left cingulate: GFAP staining shows prominent astrocytes with dilated foot processes around blood vessels. The white matter shows no significant reactive gliosis. CD68 stains macrophages in normal numbers in the meninges. There is no increase in macrophages in the grey or white matter of the brain. ßAPP shows extensive expression in a patchy or geographic distribution in which many swollen axons are seen. Myelin stain (PLP) demonstrates normal myelin. There is no evidence of myelin breakdown or myelinolysis.

Cerebellum x 2:The white matter is vacuolated but is intact. There is no myelinolysis.

Pons: The myelin is vacuolated but intact.

Hippocampus: Myelin is intact. Macrophages are not seen in the hippocampus nor is microglial activity evident. Neurones appear compressed but there is no evidence of cell death.

Right frontal: No macrophage or microglial activation is seen. Myelin is intact.

Occipital: Myelin is intact. There is no macrophage or microglial upregulation.

Aquaporin staining

Aquaporin 4 is mildly upregulated in the astrocytic foot processes of the subpial cortex and the junction of the deep cortex with the white matter. It is seen in astrocytes; in swollen foot processes around blood vessels and inoccasional very swollen cell bodies in the white matter. Aquaporin 1 is seen in a few astrocytes in the cortex and is very mildly expressed in cells at the deep cortical border.

In the cerebellum AqP4 is mainly seen in the white matter with mild expression in the molecular layer. AqP1 is seen very mildly expressed in Bergman glia of the pyramidal cell layer.

The pons shows mild AqP4 expression diffusely in the white matter and around blood vessels.

AqP4 is seen in the subpial cortex and white matter of the hippocampus. AqP1 is seen in a few cortical astrocytes.

Table 1

Case	Fresh brain weight (g)	Fixed brain weight (g)		Notes
		Whole	Hindbrain	
1	N/A	1875	200 (11%)	Brain tumour
2	1236	1285 (+3.8%)	145 (11%)	
3	N/A	948	132 (14%)	
4	1380	1462 (+6%)	148 (10%)	
5	1400	1494 (+7%)	N/A	
6	1230	1317 (+7%)	163 (12%)	
7	1248	1368 (+10%)	156 (11%)	
8	806	790 (+2%)	N/A	Old encephalitis and tissue loss
9	1224	1240 (+1%)	144 (12%)	
10	1206	1382 (+15%)	N/A	
AS	**1310**	**1680 (+28%)**	**176 (10%)**	

Reference List

Armour, A. (1997). "Dilutional hyponatraemia: a cause of massive fatal intraoperative cerebral oedema in a child undergoing renal transplantation." Journal of clinical pathology 50(5): 444-446.

Dekaban, A. S. (1978). "Changes in brain weights during the span of human life: relation of brain weights to body heights and body weights." Annals of neurology 4(4): 345-356.

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