QUERY FOR DR. SIMON HAYNES & PROFESSOR IAN YOUNG

RE: LUCY CRAWFORD

1.   Please find attached a transcript of your tele-meeting chaired by Senior Counsel to the Inquiry on Friday 28th June 2013.

2.   The transcript should be read in conjunction with the following:

- Report produced for the Inquiry by Dr. Haynes dated 21st June 2013 (**Ref: 253-002-001**)

- Inquiry Witness Statement produced by Professor Young dated 19th June 2013 (**Ref: WS-342/1**).

- Please also be aware of an addendum to Dr. Crean's Inquiry Witness Statement, containing letters in the BMJ (Volume 307, 18th September 1993, p.736) from Ellis and Arieff (**WS-292/2, p.59-60**).

3.   During the tele-meeting, you agreed to produce a joint paper for the purposes of the Inquiry addressing:

(i)   What the exercise that you were embarking on was

(ii)   What the complexities surrounding that are

(iii)   How you both approached it

(iv)   Where you are now

4.   In particular, the Inquiry would like you to address the following which were discussed during the tele-meeting:

(i)   Any changes you may wish to make to your previous calculations, and the reason(s) why you wish to make the changes.

(ii)   The calculations and the assumptions that you have used to calculate the rate of fall in Lucy's serum sodium, including the extent to which you agree with each other's calculations / assumptions, and the extent to which you disagree.

(iii) The effect of using extracellular fluid in the calculation as opposed to total body water, and the advantage / disadvantage in doing so.

(iv) Your comment on the distribution of the osmoles, and the factors affecting this.

(v) Whether, on either calculation, you consider the calculated fall in serum sodium and/or the rate of fall in the serum sodium to have been a significant fall. Further, whether you would have considered this to have been a significant fall in 2000, and whether this would be within the knowledge of specialist clinicians, i.e. experienced consultant paediatric anaesthetists / experienced consultant paediatric neurologists.

(vi) Your comment on the discussion between Ellis and Arieff in their letters to the BMJ – particularly Arieff's view that neither the magnitude nor the rate of fall in serum sodium concentration is important in the genesis of brain damage.

(vii) The issue of a possible 'idiosyncratic' response to a drop in serum sodium.

(viii) Any information you have on current research which is ongoing regarding the issue of the importance or otherwise of either the magnitude or the rate of fall in serum sodium concentration in the genesis of brain damage.

5. Please also attach any documents or articles that you consider to be relevant to this discussion and which will assist the Inquiry's understanding.

RECORDED CONVERSATION BETWEEN:
PROFESSOR IAN YOUNG & DR SIMON HAYNES

ALSO PRESENT: MS MONYE ANYADIKE-DANES QC
& MR DAVID REID BL

1   MS ANYADIKE-DANES: Hello Professor Young.

2   PROFESSOR YOUNG: Hello.

3   MS ANYADIKE-DANES: Hi, Monye Anyadike-Danes here.

4   PROFESSOR YOUNG: Hi.

5   MS ANYADIKE-DANES: Hi. And I also have with me junior counsel,

6   David Reid.

7   MR REID: Hello.

8   MS ANYADIKE-DANES: Okay. Dr Haynes, hi, how are you?

9   DR HAYNES: Good morning.

10 MS ANYADIKE-DANES: Right. Now can I just, essentially I'm just

11   trying to facilitate this discussion but I want to make sure

12   that we all have the same papers.

13   So Professor Young, you should have with you your

14   statement which incorporates, your statement is dated the 19th

15   of June 2013; it bears the reference 342-1. It has within in

16   it a number of calculations ending up with a view and

17   attaching to it a number of statements, or papers rather,

18   particularly that incorporating what has been called the

19   Adrogue formula; is that correct?

20 PROFESSOR YOUNG: Yes, that's correct.

21 MS ANYADIKE-DANES: Thank you.

22   And then Dr Haynes, we have from you a report dated the

23   21st of June 2013 and bearing the reference: 253002-001. And

24   you have appended to your report some papers, also including

25   the review of medical physiology; is that correct?

26 DR HAYNES: Yes.

27 MS ANYADIKE-DANES: And both of you have had an opportunity to look

1   at each other's papers and reports. And since then, Professor

2   Young, you have commented on Dr Haynes', if I can call it

3   modified Adrogue formula, and attached to that, and the

4   commentary which hasn't yet gone out in any formal sense, but

5   you have done it to facilitate this discussion and attached to

6   it a paper entitled: The journal of -- 'From the Journal of

7   American Heart Association'. And the title is: 'Principles of

8   Management of Severe Hyponatraemia', in due course we'll have

9   that paginated.

10   And Dr Haynes, you've had an opportunity to look at

11   that and consider it?

12 DR HAYNES: Yes.

13 MS ANYADIKE-DANES: Thank you. Then if I can say so far as I

14   understand what we're seeking to do here is for the two of you

15   to discuss the bases upon which you've approached one

16   particular issue in Lucy's case, which is to try, insofar as

17   it can be done, to express a view as to what her serum sodium

18   level was likely to have been at the point when she collapsed,

19   which is round about 3.00 am, bearing in mind that the only

20   values for her serum sodium level we have is one of 137

21   millimoles per litre which was from bloods taken at roughly

22   8 o'clock in the previous evening, and one at 127 millimoles

23   per litre which was taken from bloods at roughly 3.30, so post

24   her collapse. So those are the two values. In the

25   intervening period of time she received a quantity of low

26   sodium solution 18 fluid which started roughly at 10.30-ish,

27   and she also received a quantity of normal saline, the precise

1   start for that is unclear, as is the precise quantity. It

2   might have started at about 2.30 and gone on to have

3   administered about 500 mils by the 3.30 taking of bloods, it

4   might have been 500 mils starting immediately post crash and,

5   therefore, 500 mils in about half an hour when the bloods were

6   taken. Alternatively, it could have been 250 mils starting

7   just after her crash and then meaning that it had been

8   administered about, for about half an hour when the bloods are

9   taken. So those are the sort of unknowns that the two of you

10   are dealing with. But recognising all of that and factoring

11   in the possible variations you're trying to see if you can,

12   with any degree of reliability, come up with a serum sodium

13   level for round about 3.00 in the morning; is that understood?

14 DR HAYNES: Yes, that's fine.

15 MS ANYADIKE-DANES: Have I missed out anything?

16 DR HAYNES: I don't think so.

17 MS ANYADIKE-DANES: Professor Young?

18 PROFESSOR YOUNG: No, I think that's a very fair summary.

19 MS ANYADIKE-DANES: Right. Well if I then can go over to you,

20   gentlemen, maybe if we start from - Dr Haynes, for you to

21   explain how -- well actually maybe I think the first statement

22   came from you, Professor Young, perhaps I should correct that.

23   You had the first attempt at trying to see if you could come

24   up with a figure and that was prompted by a concern that you

25   had when the Inquiry's expert, Dr Roderick MacFaul, expressed

26   the view in his report that Lucy's serum sodium was likely to

27   be significantly lower than the 127 and you were unsure about

1   the basis of that, and I think that prompted you to do some of

2   your own calculations which ultimately we see in your

3   statement; would that be fair?

4   PROFESSOR YOUNG: Yes, that's correct.

5   MS ANYADIKE-DANES: So maybe if you can explain to Dr Haynes how

6   you went about that?

7   PROFESSOR YOUNG: Okay. So, and if I say that obviously I -- you

8   have my calculation there --

9   MS ANYADIKE-DANES: I do.

10   PROFESSOR YOUNG: -- and I have looked at interest with Dr Haynes'

11   calculation, and which certainly made me think about it in

12   some detail again. And I actually think that we have both

13   gone slightly wrong in different ways, yes. And that's why I

14   felt that this joint discussion might be helpful.

15   MS ANYADIKE-DANES: When you say you've both gone slightly wrong,

16   Professor Young, just so that, because ultimately the Chairman

17   will be reading with interest the transcript of this

18   conversation, is this an exercise that you have much

19   experience in carrying out which is to try and work back from

20   a certain circumstance what the serum sodium level in a child

21   might be?

22   PROFESSOR YOUNG: No, it's not. I am, I am quite used to employing

23   the Adrogue formula --

24   MS ANYADIKE-DANES: Yes

25   PROFESSOR YOUNG: -- or one of its derivatives --

26   MS ANYADIKE-DANES: Yes.

27   PROFESSOR YOUNG: -- to estimate the effect of saline infusion.

1   But it's clearly an unusual situation to try to work

2   backwards.

3 MS ANYADIKE-DANES: If it's any help, Dr Haynes tells me it's much

4   the same for him that this, so could I summarise it in this

5   way: This is fairly unchartered territory for both of you?

6 PROFESSOR YOUNG: Yes.

7 DR HAYNES: It is, yes.

8 PROFESSOR YOUNG: And I suspect that's the case for almost

9   everybody, to be honest, who you would talk to, because this

10   sort of retrospective analysis would not be a common exercise,

11   we're normally working prospectively.

12 MS ANYADIKE-DANES: I understand that. And that, would it be also

13   fair to say that explains some of the difficulty that the two

14   of you have had as to how you would approach it and the

15   figures that you reach?

16 PROFESSOR YOUNG: I think that's correct, yes. And Simon, would

17   you agree with that?

18 DR HAYNES: Yes, absolutely. It sounds a very simple question, and

19   it's relatively straightforward to look forward but even then

20   there's caveats when you're prospectively trying to evaluate

21   it.

22 MS ANYADIKE-DANES: Because what you're doing is modifying known

23   formula, tried and tested, but tried and tested for a

24   prospective calculation?

25 PROFESSOR YOUNG: Yes. And there are significant uncertainties in

26   those formulae. And that's why I think everybody in this area

27   recommends frequent monitoring of sodium to see the actual

1   impact.

2   MS ANYADIKE-DANES: Yes.

3   PROFESSOR YOUNG: Rather than attempting to rely on the

4   calculation.

5   MS ANYADIKE-DANES: Well thank you. If you then explain now how

6   you went about it initially and then I will ask Dr Haynes to

7   explain how he went about it initially and the two of you can

8   discuss, having seen both those attempts, what your refined

9   views are.

10 PROFESSOR YOUNG: Okay. So my starting point was the Adrogue

11   formula, and the reason I took that as the starting point, I

12   mean it was originally proposed in 1997, and continues to be

13   extensively used and it's certainly the approach I would have

14   taken in 2000 to looking at it. Now, there have been

15   modifications of the formula subsequently which attempt

16   generally to take into account urinary losses and also the

17   impact of potassium infusions. But I don't have access to the

18   information which would allow those formulae to be used so I

19   felt that the Adrogue formula was the best, the best approach

20   available to me. And I lay out my calculations in the report

21   and I don't necessarily want to go through those in --

22 MS ANYADIKE-DANES: No, no.

23 PROFESSOR YOUNG: -- in detail.

24 MS ANYADIKE-DANES: That's fine, Professor Young.

25 PROFESSOR YOUNG: What I will do is highlight where I believe my

26   calculations are incorrect --

27 MS ANYADIKE-DANES: Okay.

1 PROFESSOR YOUNG: -- on reflection. And I'm sure Dr Haynes will

2   follow this. But on the right hand side of the formula --

3 MS ANYADIKE-DANES: Can you just take us to the page --

4 PROFESSOR YOUNG: -- where we have the body water plus one.

5 MS ANYADIKE-DANES: Sorry to interrupt you, Professor Young, for

6   the purposes of referencing here can you take us to the

7   particular page in your statement.

8 PROFESSOR YOUNG: Yes, certainly. So I think this would be, I'm at

9   the top of page 5 in my report.

10 MS ANYADIKE-DANES: Yes.

11 PROFESSOR YOUNG: Let me just -- oh hang on. Oh indeed it's at the

12   bottom of page 5 as well in my report, in the pagination I

13   have which is --

14 MS ANYADIKE-DANES: Okay. It's 342-1, page 5; is that correct?

15 PROFESSOR YOUNG: Yes, I don't have the, I just have my original

16   report submitted to me, not the, not your paginated version

17   but I think that's probably correct, it's equation (a) in my

18   calculation.

19 MS ANYADIKE-DANES: Yes, little 'a', yes.

20 PROFESSOR YOUNG: Bear with me until I get to the beginning.

21 MS ANYADIKE-DANES: Sorry, just in case the Chairman should be

22   trying to follow it, the text immediately above it:

23   *"The formula can be applied to estimate the effect of infusion*

24   *of one litre of normal saline on Lucy's serum sodium*

25   *concentration in the following way".*

26   Is that the one you mean?

27 PROFESSOR YOUNG: That is the one, yes.

1   MS ANYADIKE-DANES: Yes, thank you.

2   DR HAYNES: Just tell me which bit - oh there we are. Yes, and

3   it's got A Delta --

4   PROFESSOR YOUNG: Yes.

5   DR HAYNES: -- serum sodium, yeah okay, right, yeah.

6   PROFESSOR YOUNG: So that was my starting point and it was the,

7   obviously use of one litre of fluid.

8   MS ANYADIKE-DANES: Uh-huh.

9   PROFESSOR YOUNG: And I think that actually both Dr Haynes and

10   myself have done that calculation for one litre of fluid in

11   the same way and came essentially to the same result, the

12   difference being the assumption we made around total body

13   water.

14   DR HAYNES: Yes.

15   PROFESSOR YOUNG: Now where I think we both subsequently went wrong

16   in slightly different ways was in trying to correct the

17   calculations to allow for 500 mils or 250 mils of fluid.

18   DR HAYNES: Yes, I think we've gone wrong in --

19   PROFESSOR YOUNG: So it's my --

20   DR HAYNES: -- different mistakes at that point.

21   PROFESSOR YOUNG: Yes. So my mistake was I retained TBW + 1 and --

22   DR HAYNES: Uh-huh?

23   PROFESSOR YOUNG: And I should have amended that to TBW + 0.5.

24   MS ANYADIKE-DANES: Uh-huh.

25   PROFESSOR YOUNG: Or TBW + 0.25.

26   DR HAYNES: Yes.

27   PROFESSOR YOUNG: Now, along with doing that you then need to make

1   an additional correction which is on the lower part of the

2   equation on the right, you need to introduce a factor which

3   allows division, so for 500 mils you would end up on the

4   bottom line of the equation with 2 (TBW + 0.5). And for 250

5   --

6 DR HAYNES: Sorry, could you say that again?

7 PROFESSOR YOUNG: So to allow for the facts, so the formula on the

8   right, the Delta relates to one litre --

9 DR HAYNES: Uh-huh?

10 PROFESSOR YOUNG: -- and to allow for the 500 mils you need to make

11   an additional modification on the right which means that on

12   the denominator, the bottom line, you have 2 (TBW + 1) --

13   sorry (TBW + 0.5).

14 DR HAYNES: Ah yes, that - oh yes.

15 PROFESSOR YOUNG: When do you do it for 250 mils it is 4 (TBW +

16   0.25).

17 DR HAYNES: And then you can solve it for the desired amount?

18 PROFESSOR YOUNG: Yes.

19 DR HAYNES: Yes.

20 PROFESSOR YOUNG: So that's what I -- now that I believe is the

21   error that I made and that actually --

22 MS ANYADIKE-DANES: So was that --

23 PROFESSOR YOUNG: -- is the, would be the correct way of

24   approaching it.

25 MS ANYADIKE-DANES: Does that mean, Professor Young, when you were

26   setting out your initial formula, or at least your initial

27   equation you had not factored appropriately into it the two

1   different amounts of normal saline that she got which you're

2   trying to neutralise the effect of for the purposes of working

3   out where she was at 3.00, which is on the one hand she either

4   got 250 mils of it or on the other hand she got 500 mils of

5   it?

6 PROFESSOR YOUNG: So it's not quite that. What I did was to work

7   out the effect for 1 litre --

8 MS ANYADIKE-DANES: Yes.

9 PROFESSOR YOUNG: -- as Dr Haynes did.

10 MS ANYADIKE-DANES: Yes.

11 PROFESSOR YOUNG: And then I, after having done that I divided the

12   effect by 2 or by 4 to work out the effect of 500 and 250.

13 MS ANYADIKE-DANES: Uh-huh.

14 PROFESSOR YOUNG: So I did factor them in, but I factored them in

15   at the end.

16 MS ANYADIKE-DANES: I see, I see, yes.

17 PROFESSOR YOUNG: And mathematically that was slightly

18   inappropriate.

19 MS ANYADIKE-DANES: Okay, I see.

20 DR HAYNES: Okay.

21 PROFESSOR YOUNG: The slightly modified version I have given is, I

22   think, the correct way of doing it. In fact the differences

23   compared with the numbers I calculated are actually pretty

24   small, but the way I did it was slightly incorrect.

25 MS ANYADIKE-DANES: Okay.

26 DR HAYNES: Yes. Can I, maybe it might help, if I just outline

27   where I think I went wrong at that stage.

1   MS ANYADIKE-DANES: Okay.

2   DR HAYNES: I looked at the formula and assumed incorrectly that

3   the + 1 was giving the correct sum for giving 1 litre.

4   MS ANYADIKE-DANES: If you're going to particular part in your

5   report, Dr Haynes, can you tell us where it is for referencing

6   purposes.

7   DR HAYNES: Right, hold on. So we're still at the same point in

8   Professor Young's report?

9   MS ANYADIKE-DANES: Yes.

10 DR HAYNES: Right. So starting at the lower half of page 4.

11 PROFESSOR YOUNG: Yes, I've got that.

12 DR HAYNES: So --

13 MS ANYADIKE-DANES: Which is 253002004.

14 DR HAYNES: Yes, that's it, yeah, okay. So it's the bit that

15   starts: The formula is, changes to serum sodium, which is

16   basically the Adrogue formula written longhand. So then the

17   little paragraph explaining as applied. Now the mistake that

18   I have made is I have said the Adrogue formula is adding 1

19   litre and that 1 litre goes in the denominator on the right

20   hand side as a + 1.

21 MS ANYADIKE-DANES: Uh-huh.

22 DR HAYNES: And I've made the mistake of saying: Whoa, we're not

23   doing that, we're taking off 0.5, 0.25 --

24 MS ANYADIKE-DANES: Uh-huh.

25 DR HAYNES: -- and haven't checked the whole thing through. And

26   when it was the numbers for Lucy and it made some sort of

27   sense I thought great, I've done it. And then Professor Young

1   came back saying: If you put these numbers in it makes

2   nonsense, which in fact it does. So I made an invalid

3   arithmetical or algebraic assumption about how the denominator

4   on the right hand side of the Adrogue formula could be

5   adapted.

6 MS ANYADIKE-DANES: And why were you trying to adapt it like that?

7 DR HAYNES: Because the Adrogue formula specifically said: If you

8   give one litre of fluid this is what we think is 'going',

9   future tense, to happen.

10 MS ANYADIKE-DANES: Uh-huh.

11 DR HAYNES: I then took the formula and said: If we, we're not

12   giving one litre of fluid, we're trying to say what's

13   happening when you take away either 500 mils or 250 mils and

14   look back in time.

15 MS ANYADIKE-DANES: Uh-huh.

16 DR HAYNES: And it's not as simple as that.

17 MS ANYADIKE-DANES: Okay. So the both of you have tried to work

18   retrospectively and calculate for 3.00 am, both with some

19   application or modification of the Adrogue formula. Both of

20   those uses didn't help you ultimately get to what you consider

21   to be a likely accurate figure, albeit within bracket, within

22   bounds if I could say. So then the next step is, Professor

23   Young, what do you do now?

24 MS ANYADIKE-DANES: No, sorry if I can just go to you, Professor

25   Young, as to how you, once you have reached that was

26   inappropriate, okay, and you have now recalculated it as you

27   have done?

1   PROFESSOR: Yes -- no, no --

2   MS ANYADIKE-DANES: Is that the - so go ahead.

3   PROFESSOR YOUNG: -- the mistake which I made I think has actually

4   very limited impact but whenever I rerun it and do it in what

5   I believe to be the correct way then in the case of 500 mils

6   --

7   MS ANYADIKE-DANES: Yes.

8   PROFESSOR YOUNG: -- I came up with the initial sodium 124.3.

9   MS ANYADIKE-DANES: Uh-huh.

10   PROFESSOR YOUNG: So just over 124.

11   MS ANYADIKE-DANES: Yes.

12   PROFESSOR YOUNG: Which is actually what I said before but I was a

13   little, you know, it was just not done correctly

14   mathematically.

15   MS ANYADIKE-DANES: Okay. And for 250?

16   PROFESSOR YOUNG: When I run the calculation for 250 mils I came up

17   with 125.7 which is just under 126 basically because the lab

18   would report it to the nearest single digit.

19   MS ANYADIKE-DANES: Yes.

20   PROFESSOR YOUNG: So again it's actually the same figures I came up

21   with before but the decimal places are different.

22   MS ANYADIKE-DANES: Okay. So is that now what you consider to be a

23   reasonable level for 3, for the 3 o'clock?

24   PROFESSOR YOUNG: Well that's what I consider to be a reasonable

25   level based on the Adrogue formula and we may, we may come on

26   to the other --

27   MS ANYADIKE-DANES: Yes, so let's --

1   PROFESSOR YOUNG: -- other options. But based on the Adrogue

2   formula that's what I consider to be a reasonable level.

3   MS ANYADIKE-DANES: Thank you.

4   PROFESSOR YOUNG: Depending on whether it was 250 or 500.

5   MS ANYADIKE-DANES: I understand.

6   Now Dr Haynes, if I come to you now, you were working

7   with a sort of a revised or a modified version of the Adrogue

8   formula. When you recognised from what Professor Young had

9   done that you also perhaps in your modification had not used

10   it in a way to replicate as best as possible what you think

11   happens and therefore to give you an appropriate level; do you

12   either accept this modification that Professor Young has made

13   or have you got some other view as to how you could use the

14   Adrogue formula?

15 DR HAYNES: I think, was it - this is the first time I've heard or

16   seen Ian's modification of the Adrogue formula.

17 MS ANYADIKE-DANES: Okay.

18 DR HAYNES: I think it's possibly a mistake even to try and use the

19   Adrogue formula because we're trying to modify something that

20   wasn't designed to be used this way.

21 MS ANYADIKE-DANES: Well if I pause there just so that we have it

22   for clarity, does that mean that you're not certain that even

23   this modification from that which Professor Young had

24   previously tendered helps us?

25 DR HAYNES: I think it's an improvement on what went before, but I

26   have thought subsequently about it and I think there's

27   possibly a better way which I elaborated in my discussion

1   paper yesterday of trying to approach this.

2 MS ANYADIKE-DANES: Okay.

3 DR HAYNES: Which I now feel more comfortable with and I have

4   realised that it's something actually I use fairly frequent in

5   day to day clinical practice.

6 MS ANYADIKE-DANES: And so does, now just again so that we're

7   clear, before we move from the Adrogue formula at all do you

8   consider the modification to be as far you can go or an

9   appropriate modification of the Adrogue formula?

10 DR HAYNES: Yes, I can't see any way it could be improved for this

11   situation.

12 MS ANYADIKE-DANES: So that's the best that you can get out of the

13   Adrogue formula. And then does the question become whether

14   that is still an appropriate way of approaching the problem?

15 DR HAYNES: Yes.

16 MS ANYADIKE-DANES: Okay. Well then if I ask you then to develop

17   that. You don't think that it is, clearly from what you said,

18   so firstly can you explain why you don't think it is and what

19   you think the appropriate way of approaching the problem

20   should be now?

21 DR HAYNES: Right. Well, it's dawned on me that there's actually a

22   simpler way of approaching it.

23 MS ANYADIKE-DANES: Well firstly can we deal with the first thing,

24   why you don't think that that is an appropriate way of

25   approaching the problem?

26 DR HAYNES: I think it, that using the Adrogue formula which is

27   very specific in what it is designed to do --

1 MS ANYADIKE-DANES: It might help us with what that is?

2 DR HAYNES: Right. The author's Adrogue and the other guy who came

3   up with it are very specific and they say: This is what we

4   think is likely to happen if you give a litre of the following

5   sodium concentration to a patient. And anything, and any

6   modification we do will not have had the same testing, if you

7   like, these authors put into developing the Adrogue formula --

8   -

9 MS ANYADIKE-DANES: Okay.

10 DR HAYNES: -- and we're trying to arithmetically correct for a

11   different volume and I think, and the -- if you're looking at

12   different volumes, and we have now 250 mils or 500 mils, if

13   you mix 250 mils or something with this circulation it will

14   cause a different increment to the subsequent 250 mil

15   identical I think to what was added. So we're trying, and

16   correct me if I'm wrong, I'm old enough to be corrected, we're

17   dividing a linear, or using the modification of the Adrogue

18   formula to produce a linear effect where it's not actually

19   linear because if you're giving normal saline to somebody

20   who's hypotonic, the first few mils will have much more of a

21   change on the sodium than will subsequent mils and that's

22   quite an easy calculation to run through.

23 MS ANYADIKE-DANES: Okay.

24 DR HAYNES: So any derivation of the Adrogue formula which is

25   immediate to linear is going to be flawed, and I'm not sure

26   how big that flaw is going to be, it may be trivial or it may

27   be significant. So that thought makes me feel a little

1   uncomfortable about using any derivation, however well derived

2   it is.

3 MS ANYADIKE-DANES: So then if you can explain what, recognising

4   what you consider to be the deficiencies in using even a

5   modified version of the Adrogue formula, what was the approach

6   that you used to try and get the figure for 3.00?

7 DR HAYNES: Well it dawned on me that looking prospectively at this

8   kind of problem is something that in a completely different

9   context I deal with regularly and it so happens that the paper

10   from drama with its list of equations, number 7 comes out with

11   something that is used in, that, you know, I use pretty

12   regularly in clinical practice. And --

13 MS ANYADIKE-DANES: Well just let's just be clear of the paper that

14   you're talking about --

15 DR HAYNES: Yes --

16 MS ANYADIKE-DANES: -- is that: The principles of management of

17   severe hyponatraemia --

18 DR HAYNES: That's Antonios H Tzamaloukas et al, originally

19   published January 23rd, 2013.

20 PROFESSOR YOUNG: Yes, I mean I have certainly found the space and

21   I've got it here.

22 DR HAYNES: Well you've got the actual proper reference.

23 MS ANYADIKE-DANES: Don't worry, Dr Haynes, we will paginate this

24   and give the reference, but if for the moment you deal with

25   the internal page numberings from the paper that Professor

26   Young provided.

27 DR HAYNES: Okay. If you then go to page 4 of the --

1   MS ANYADIKE-DANES: Yes.

2   DR HAYNES: -- journal paper, and you look at the various equations

3   which are thought through ...

4   MS ANYADIKE-DANES: Under table 2?

5   DR HAYNES: Yes, under the list of formulas. And if you then go to

6   equation number 7 --

7   MS ANYADIKE-DANES: Uh-huh.

8   DR HAYNES: -- it then becomes very simple to rearrange that

9   equation and then solve it for Na INE which is the initial

10   sodium concentration which is what we're trying to work out.

11 MS ANYADIKE-DANES: Okay.

12 DR HAYNES: And that's what I did yesterday afternoon in generating

13   this paper and it dawned on me that it was appropriate because

14   the principles are the same as what happens when you connect a

15   child who's having heart surgery to a cardiopulmonary bypass

16   machine which contained fluid which mixes pretty much

17   instantly with a child in circulation when they go on bypass.

18   And it's something that we mentally run through pretty quickly

19   what the likely impact, if any, of the components of the two

20   circuit -- of the two pots of the circulation when mixed will

21   do.

22 MS ANYADIKE-DANES: Sorry, just for the sake of others trying to

23   follow this, when you say what it's likely to do does that

24   mean you need to know that if they're likely because of the

25   difference between the two to be any great oscillations in

26   doing it that you know what the parameters of those

27   oscillations are and you know that they are appropriate and

1   safe as well as --

2 DR HAYNES: Yes.

3 MS ANYADIKE-DANES: -- what your likely equilibrium point will be?

4 DR HAYNES: Yes.

5 MS ANYADIKE-DANES: Okay.

6 DR HAYNES: So, for example, if you were to have an extreme

7   situation where you, say, had a 10 kilogramme child coming for

8   heart surgery and there's about 758/800 mils of fluid in the

9   bypass, if all of that was 5% glucose you could see that

10   instantly there would be a very rapid decrease in serum sodium

11   within that child.

12 MS ANYADIKE-DANES: Okay.

13 DR HAYNES: And that's an extreme example, but it's a mistake that

14   has been made and you have to make sure that it's not going to

15   happen.

16 MS ANYADIKE-DANES: So then if you rearrange the formula to try and

17   account for the exercise that you and Professor Young have

18   undertaken --

19 DR HAYNES: Uh-huh.

20 MS ANYADIKE-DANES: -- what does that then - or are you able to

21   explain that in a way that Professor Young can follow and then

22   say what that produces either on the basis of 500 mils or 250

23   mils of normal saline?

24 DR HAYNES: Right. So if you've got the paper I sent you yesterday

25   in front of you?

26 MS ANYADIKE-DANES: I'm not sure that Professor Young's got that.

27 PROFESSOR YOUNG: No, I don't have that, no.

1   DR HAYNES: Okay.

2   MS ANYADIKE-DANES: Right, then you might have to explain -- well

3   you will have to explain that to him.

4   DR HAYNES: Right, okay. So I'll go through it step by step.

5   Right well if you take the formula from that table 2 of that

6   paper, formula number 7.

7   PROFESSOR YOUNG: Yes.

8   DR HAYNES: That, if you put that down on paper, that gives you the

9   final sodium concentration which we know is 127.

10 PROFESSOR YOUNG: Yes.

11 DR HAYNES: Equals (the initial total body water x the initial

12   sodium concentration --

13 PROFESSOR YOUNG: Yes.

14 DR HAYNES: --) +.

15 PROFESSOR YOUNG: Yes.

16 DR HAYNES: (The volume of the fluid given, plus the sodium

17   concentration --

18 PROFESSOR YOUNG: Yes.

19 DR HAYNES: -- in that. And as a denominator you have the initial

20   total body water plus the volume infused.

21 PROFESSOR YOUNG: Yes. Okay.

22 DR HAYNES: So you then rearrange that equation.

23 PROFESSOR YOUNG: Uh-huh?

24 DR HAYNES: Such that the denominator on the right comes up to

25   multiply the numerage on the left, you get final sodium

26   concentration x total body water initial).

27 PROFESSOR YOUNG: Yes.

1   DR HAYNES: Add (final sodium x volume infused).

2   PROFESSOR YOUNG: Yes.

3   DR HAYNES: Equals initial total body water + initial sodium

4   concentration, which is the magic X, we're trying to find

5   that.

6   PROFESSOR YOUNG: So it's the initial total body water times or

7   plus?

8   DR HAYNES: It's times.

9   PROFESSOR YOUNG: Yes, okay, yes.

10 DR HAYNES: Okay. Close brackets, plus sign.

11 PROFESSOR YOUNG: Yes.

12 DR HAYNES: (Volume infused + sodium concentration that was

13   infused.

14   So please tell me if I made an algebraic error in rearranging

15   that?

16 PROFESSOR YOUNG: No, that sounds okay. Yes.

17 DR HAYNES: I worked it out 10 times yesterday and (inaudible). I

18   almost got my son to get his GCE Master.

19 PROFESSOR YOUNG: Okay, that sounds all right, yes.

20 DR HAYNES: Right. So Monye, if you go to the paragraph above

21   that, at the beginning of that page.

22 MS ANYADIKE-DANES: Yes, I'm with you.

23 DR HAYNES: Do you have that in front of you?

24 MS ANYADIKE-DANES: Yes, I've got you.

25 DR HAYNES: So I've got a little heading which says: "*Lucy;*".

26 MS ANYADIKE-DANES: Yes.

27 DR HAYNES: Yes?

1 MS ANYADIKE-DANES: Uh-huh.

2 DR HAYNES: Weight = 9.14 kilos, and then two different potential

3   estimates for her total body water.

4 MS ANYADIKE-DANES: Okay.

5 DR HAYNES: One of which is, assumes 10% dehydrated and one of

6   which assumes that 9.14 is her healthy weight.

7 MS ANYADIKE-DANES: Okay.

8 DR HAYNES: As it turns out using this formula it doesn't matter

9   that much which you use.

10 PROFESSOR YOUNG: Yes.

11 DR HAYNES: Okay. Then the volume infused we know to be either .5

12   or .25 litres.

13 PROFESSOR YOUNG: Yes.

14 DR HAYNES: Sodium concentration of what's given is 154 millimoles

15   per litre.

16 PROFESSOR YOUNG: Yes.

17 DR HAYNES: We know that the final sodium is 127.

18 PROFESSOR YOUNG: Yes.

19 DR HAYNES: And we need to --

20 MS ANYADIKE-DANES: The initial sodium?

21 DR HAYNES: For the initial sodium.

22 PROFESSOR YOUNG: Yes.

23 DR HAYNES: Happy?

24 PROFESSOR YOUNG: Yes.

25 DR HAYNES: Okay. Now, the equation says: "*Use total body water*",

26   and this is where you have raised an eyebrow and said: 'Look

27   here, come on'. Let me just run through this. Now what I

1   think we're trying to do is to find the possible nadir in

2   Lucy's sodium serum.

3 PROFESSOR YOUNG: Yes.

4 DR HAYNES: Now, conventionally you'd run it through using values

5   for total body water, but that is what it's going to be after

6   what you've given has had a chance to equilibrate and

7   redistribute throughout, through the various fluid

8   compartments of the body.

9 PROFESSOR YOUNG: Yes.

10 DR HAYNES: What it doesn't do is say if you suddenly gave ebolas

11   what's the swing going to be, what's the potential peak swing.

12   My argument, and please feel free to criticise it robustly if

13   you think I'm going the wrong direction, is let's assume for

14   the sake of argument that the saline was given very quickly,

15   mixed only with the blood, which we can -- which, and I have

16   just used extracellular fluid for that, and then subsequently

17   had a chance to redistribute.

18 PROFESSOR YOUNG: Yes.

19 DR HAYNES: Now it's not going to be instantaneous, it's going to

20   be somewhere between the two limits, I think, will give a

21   reasonable guesstimate for the range we're talking about. But

22   I have done it with that calculation really because you have

23   to, I feel you have to start from somewhere.

24 PROFESSOR YOUNG: Okay, so just so as I'm clear, and I do actually

25   follow the argument, and I suppose my view has been that the

26   redistribution of the osmoles, which is what occurs rather

27   than the sodium, would occur very rapidly indeed, that's my

1   view, but I recognise actually there is probably space for

2   different opinions on this and presumably you can run the

3   calculation for total body water and then run it separately

4   for extracellular --

5 DR HAYNES: Yes.

6 PROFESSOR YOUNG: -- and obviously this is what you did at the

7   first --

8 DR HAYNES: I have run it through eight times.

9 PROFESSOR YOUNG: Yes.

10 MS ANYADIKE-DANES: So Dr Haynes, sorry can I just pause there.

11 DR HAYNES: Yes.

12 MS ANYADIKE-DANES: Professor Young has said well, he would have

13   assumed that that distribution, the equilibrium for the

14   osmoles would happen quite speedily, can we deal with that

15   first. Can you say whether you agree with that or, and/or

16   whether you think there are factors that might affect the

17   speed with which that distribution occurs?

18 DR HAYNES: Yes. Now, if I can look, and again I'm going back to

19   daily clinical practice and going back to my area of, well

20   from the operating theatre with kids having heart surgery

21   using a bypass circuit. If now we invariably will measure

22   point of care testing, basic laboratory stuff which includes

23   electrolytes, and a diffusionist will do the same on his pot

24   of fluid which is in the bypass pump, and he'll come along and

25   say: 'Simon, is this all right'? And if there's a bit of a

26   discrepancy we'll quite often do a quick calculation just

27   using blood volume and the volume in the pump to guess what

1   the result might be when the two are mixed together. Now if

2   you actually look, and I've not documented it over the years

3   unfortunately, but it might interest an audit project which is

4   another aside, if you were then to take a sample pretty

5   quickly after the two volumes were mixed and then the volume

6   at various times subsequently, if there was a discrepancy

7   between the two volumes of fluid to begin with, it's much more

8   pronounced initially than it is an hour later or the next

9   result is different to what it is an hour later when you

10   really do have a pretty closed circuit, apart from your own

11   analysis.

12 PROFESSOR YOUNG: So I think I follow that, and I mean all I can,

13   all I can say is I actually haven't, I was very interested in

14   the point that Dr Haynes made and I had a look, I can't find

15   any experimental data --

16 DR HAYNES: There's not.

17 PROFESSOR YOUNG: -- to show how, to measure sodium very rapidly

18   when you're infusing saline into somebody with hyponatraemia.

19 DR HAYNES: Uh-huh.

20 PROFESSOR YOUNG: Actually I think it's a very interesting research

21   question, we'll maybe talk about it separately at some point.

22 MS ANYADIKE-DANES: You will have to join the list, Professor

23   Young, we have a number of them that this Inquiry has

24   generated.

25 PROFESSOR YOUNG: Yes. You know we can talk about looking at it,

26   my assumption was that because effectively cellular membranes

27   are semi-permeable in terms of osmolality --

1 DR HAYNES: Uh-huh.

2 PROFESSOR YOUNG: -- that their redistribution would occur very

3   rapidly, and I would personally have guessed over the course

4   of a couple of minutes, but I don't know that.

5 DR HAYNES: And I don't know whether I'm going to find the other

6   extreme.

7 PROFESSOR YOUNG: Yes. So we're into an area, a grey area, but I'm

8   very happy that we look at the calculation done in the two

9   ways.

10 MS ANYADIKE-DANES: Okay.

11 PROFESSOR YOUNG: And then, you know, provide a range, that seems

12   to me reasonable and kind of outline the limitations of, and

13   why it's being done in that way.

14 DR HAYNES: Okay.

15 MS ANYADIKE-DANES: Okay.

16 DR HAYNES: Right, are you ready?

17 PROFESSOR YOUNG: Yes, I am.

18 DR HAYNES: Right. First of all, are you okay with using this

19   equation to try and, well, to try and solve this equation?

20 PROFESSOR YOUNG: Yes, I mean I need to sit down but I think I am,

21   but I mean I think this is just, this is a derivation of the

22   Adrogue formula so I'm kind of assuming at this point it will

23   probably give a similar result with total body water, although

24   I don't know so --

25 DR HAYNES: Yes. Maybe I'm being a bit safe here but I just find

26   that I'm more comfortable with this.

27 PROFESSOR YOUNG: Yes.

1   DR HAYNES: Right, okay. Are you sitting comfortably for eight

2   running, run throughs of this?

3   PROFESSOR YOUNG: Yes, I'm ready.

4   DR HAYNES: Right. The first time I have run through it, or run it

5   through where the total body water is estimated as 4.75

6   litres.

7   PROFESSOR YOUNG: Okay.

8   DR HAYNES: Which tends to be dry.

9   PROFESSOR YOUNG: Yes.

10 DR HAYNES: And we give half a litre of normal saline.

11 PROFESSOR YOUNG: Yes.

12 DR HAYNES: Run that through and we find that the initial sodium

13   comes out as 124.0.

14 PROFESSOR YOUNG: Yes, that's fine.

15 DR HAYNES: Okay?

16 PROFESSOR YOUNG: Yes.

17 DR HAYNES: (b) assume that she's not dehydrated and there's a

18   larger total body water.

19 PROFESSOR YOUNG: Uh-huh.

20 DR HAYNES: And you again give half a litre.

21 PROFESSOR YOUNG: Yes.

22 DR HAYNES: Run it through and it comes out at 124.5.

23 PROFESSOR YOUNG: Yes, that's fine.

24 DR HAYNES: (c) assume she is a bit dehydrated, 4.57 litres total

25   body water, and you give 250 mils.

26 PROFESSOR YOUNG: Yes.

27 DR HAYNES: You come through at 125.6.

1   PROFESSOR YOUNG: Yes, that's fine.

2   DR HAYNES: And (d) assume she's not dehydrated, again you give a

3   quarter of a litre, 125.8.

4   PROFESSOR YOUNG: Yes.

5   DR HAYNES: So they're the same figures that you've generated

6   really; aren't they?

7   PROFESSOR YOUNG: Yes. So they are exactly the same figures, I

8   think, I mean I think this is the same calculation as the one

9   I presented at the start of the discussion this morning, the

10   correct use of the Adrogue.

11 DR HAYNES: Yes.

12 PROFESSOR YOUNG: I think basically. So I think those are the same

13   figures that you would get from that.

14 DR HAYNES: Certainly, or they point at something differently than

15   they are.

16 PROFESSOR YOUNG: And that's because your body water is different.

17   And I think if I put in your body water figures I would get

18   exactly the same numbers.

19 DR HAYNES: Yes. And if I put in yours, I'll get yours, yes.

20 PROFESSOR YOUNG: Yes, yes, that's about it.

21 DR HAYNES: Right. Phew! Easy so far. Now, here enters the

22   elephant in the room. If you run through the whole sequence

23   again but do it just for an approximation of extracellular

24   fluid --

25 PROFESSOR YOUNG: Yes.

26 DR HAYNES: -- this is where you get way different numbers.

27 PROFESSOR YOUNG: Yes, absolutely.

1   DR HAYNES: So without, do you want them all or can I just say the

2   range?

3   PROFESSOR YOUNG: Well no, well you can just, I mean I'll assume

4   they are either in the same order, just run me down the four

5   numbers.

6   DR HAYNES: Right, okay. Where you're dry and you give half a

7   litre.

8   PROFESSOR YOUNG: Yes.

9   DR HAYNES: And it comes out 118.1.

10 PROFESSOR YOUNG: Yes.

11 DR HAYNES: Where she's not dehydrated and you give half a litre,

12   it comes out at 119.6.

13 PROFESSOR YOUNG: Yes.

14 DR HAYNES: The next one is where she's dry and you give her a

15   quarter of a litre.

16 PROFESSOR YOUNG: Yes.

17 DR HAYNES: It comes out at 122.6.

18 PROFESSOR YOUNG: Yes.

19 DR HAYNES: And where she's not dry and you give a quarter of a

20   litre it comes out at 123.3.

21 PROFESSOR YOUNG: Yes. No, I'm absolutely happy with the, I mean I

22   haven't done the calculations in detail but those numbers seem

23   entirely reasonable and I'm happy with the approach. So the

24   key is the extent to which you assume that the sodium

25   distributes in total body water or extracellular only?

26 DR HAYNES: Yes. So it's how we choose to interpret it.

27 PROFESSOR YOUNG: Yes. And I mean and if I kind of comment just

1   generally, I mean I, just to be clear my own view would have

2   been, and is, that even if the sodium were 126/127 as the

3   lowest, that that would have been low enough to lead to the

4   cerebral oedema in this case.

5 DR HAYNES: Yes.

6 PROFESSOR YOUNG: Given the rate of the fall.

7 DR HAYNES: Yes --

8 MS ANYADIKE-DANES: Sorry, Professor Young, can I just ask you to

9   pause there a minute and help us with this because you know

10   from your involvement in the Claire case --

11 PROFESSOR YOUNG: Yes.

12 MS ANYADIKE-DANES: -- that we're always trying to deal with what

13   you can reasonably expect, even specialist consultants to have

14   known at the relevant time. So the relevant time is 2000 for

15   specialist consultants, by that I mean experienced paediatric

16   consultant anaesthetist or experienced paediatric consultant

17   neurologist, so that's the skill set we're dealing with and

18   we're dealing with their likely knowledge in 2000. So when

19   you say well if it had been 126 or 127 in your view that would

20   have been sufficient to have indicated that that was likely to

21   have had some contributory factor to the development of her

22   fatal cerebral oedema. And when you say that are you saying

23   that from 2000 or are you saying that from 2013?

24 PROFESSOR YOUNG: Well, I'm saying that from 2000 but from the

25   perspective of a consultant clinical chemist.

26 MS ANYADIKE-DANES: Okay.

27 PROFESSOR YOUNG: With a significant interest in the area.

1   MS ANYADIKE-DANES: So you would have thought that --

2   PROFESSOR YOUNG: And actually I'm going to defer to Dr Haynes and

3   the other expert paediatricians in terms of what would have

4   been reasonable knowledge on the part of, you know, we're

5   consulting various paediatric specialities at that time.

6   MS ANYADIKE-DANES: Okay, so if we leave out what would have been

7   the reasonable knowledge and stay with your discipline then.

8   PROFESSOR YOUNG: Yes.

9   MS ANYADIKE-DANES: So from your point of view if I were asking

10   you: Professor Young, what is your view on the likely effect

11   or contribution to the development of a fatal cerebral oedema

12   of a rate of fall in serum sodium from 137 to 126 or 127,

13   whatever at that point your calculations show it to be, over a

14   period of let us say four and a half to five hours; how would

15   you have answered that?

16 PROFESSOR YOUNG: So my view would have been that that magnitude of

17   fall over that time period would be sufficient to cause

18   cerebral oedema in some individuals.

19 MS ANYADIKE-DANES: Yes.

20 PROFESSOR YOUNG: But that many might tolerate that without

21   problem, and this comes back to the issue of the

22   idiosyncricity which I know has been discussed elsewhere by

23   the Inquiry but certain --

24 MS ANYADIKE-DANES: In your experience, Professor Young, when you

25   say in some individuals, are you saying that because in your

26   experience that is the case and so the idiosyncricity is not a

27   hypothetical, it's something that you do have experience of

1   and the concern then begins to see whether you can anticipate

2   whether you have, or even work out after the fact whether

3   you've had a patient who was likely to respond in a more

4   sensitive way, if I can use it in lay terms, than another?

5   PROFESSOR YOUNG: Yes, so I have actual experience in my

6   observation of idiosyncricity or individual variation is based

7   on observation and experience.

8   MS ANYADIKE-DANES: I see.

9   PROFESSOR YOUNG: But certainly from my speciality point of view

10   that magnitude of fall over that period of time in a child

11   would have rung alarm bells in 2000. Whether or not the child

12   was actually symptomatic I would have wanted to intervene --

13   MS ANYADIKE-DANES: I understand. So whether or not you have

14   sufficient information about the child to work out that that

15   is actually what is happening with the child, if you knew

16   about that rate of fall you would want to do some further work

17   to ascertain what actually was happening with that child,

18   because that's enough for you to be concerned?

19   PROFESSOR YOUNG: Yes, and I would have wanted to intervene to

20   prevent a further fall, I would have been concerned about the

21   potential impact of that fall.

22   MS ANYADIKE-DANES: Thank you very much, Professor Young.

23   So if I then come to you, Dr Haynes. Professor Young

24   has got his figure, or at least what he thinks the nadir to be

25   is 126/127, in other words not terribly different from what

26   the figure was from the bloods taken after that administration

27   of normal saline, whatever it turns out to be. You, I think,

1   are slightly lower than that; is that right?

2 DR HAYNES: I'm slightly lower but if we stick with what we

3   absolutely know and we know that it was 127 or possibly less

4   and just, if I was a doctor in round about 2000 when Lucy came

5   into the hospital we know that her sodium was 137 and I think

6   it would be a safe assumption to say that it didn't change

7   between then and when the administration of hypertonic fluid

8   began.

9 MS ANYADIKE-DANES: Okay. Well would you agree with that,

10   Professor Young?

11 PROFESSOR YOUNG: Yes, yes, I think so. It wouldn't have been a

12   significant change, yes.

13 MS ANYADIKE-DANES: Okay.

14 DR HAYNES: So it would still have been 137 or thereabouts because

15   it was half past ten or so when the fluid was started.

16 MS ANYADIKE-DANES: Yes, and the significance of that assumption is

17   because it changes and makes more concentrated the period over

18   which the fall occurs.

19 DR HAYNES: Yes.

20 MS ANYADIKE-DANES: Okay.

21 DR HAYNES: Okay. So it drops 10 and as a rule of thumb, and I

22   don't quite know where the rule of thumb has come from, any

23   change of more than 3 in any given hour raises an eyebrow and

24   makes one want to look and correct because of the risk of

25   there being consequences of hyponatraemia or a shift in serum

26   sodium.

27 MS ANYADIKE-DANES: Yes.

1   DR HAYNES: So I would have said in 2000 it, at the very least,

2   deserved serious consideration.

3   MS ANYADIKE-DANES: What do you mean by serious consideration, do

4   you mean further investigation --

5   DR HAYNES: Yes --

6   MS ANYADIKE-DANES: -- action taken to try and stop it?

7   DR HAYNES: If I was looking at this from the Belfast Sick

8   Children's Hospital as a consultant --

9   MS ANYADIKE-DANES: Uh-huh.

10 DR HAYNES: -- and Lucy being brought to me and we had a child who

11   had a seizure and a coma, with nothing else other than what

12   sounds like relatively mild gastroenteritis, and there's some

13   fluid administration, why on earth should the child such as

14   that develop such a catastrophic neurological injury? What on

15   earth has gone on? It's not a trivial thing, and it's

16   ultimately killed her. And you do know at a point in time

17   that it may well kill her, or have killed her. If you look

18   at, looking at the evidence in front of you the only thing

19   that rears its head and says: 'Look at me' is this change in

20   serum sodium, 137 to one hundred and (inaudible) over a

21   relatively short period of time, that can't be ignored. That

22   can't be just dismissed as oh it's an artefact or it is of no

23   consequence. That sits up and says: Please look at me, look

24   what's gone on with this child, unpick this. So knowing that

25   there was a drop of 10 would make me concerned to try and get

26   to the bottom of it all.

27 MS ANYADIKE-DANES: And Professor Young, do you have a view of what

1   Dr Haynes has just said?

2 PROFESSOR YOUNG: I mean I'm, I would be largely in agreement with

3   that, I mean if I had been asked to see this child at the time

4   or consulted I would certainly have been very concerned about

5   the sodium and would have felt that that needed followed up.

6   I mean in the previous case where I had involvement with

7   Claire Roberts there were other pathologies which might

8   possibly have explained what had happened.

9 MS ANYADIKE-DANES: Yes.

10 PROFESSOR YOUNG: But in this case I couldn't see any other

11   pathology from the information I was aware of so I would have

12   been very very concerned about the sodium in this case.

13 MS ANYADIKE-DANES: Thank you.

14   And then if we just go back to, that's where you have

15   converged because you're both looking at it from the point of

16   view of 127 and in a way you're looking at that (1) because

17   that's actually the measured figure, (2) because, Professor

18   Young, your calculations have gone to show you that that's

19   what she, that was likely to have been her lowest point or

20   something not very far off that?

21 PROFESSOR YOUNG: I think what my calculations suggest if we accept

22   that she got 500 mils of saline before the measurement then my

23   calculation would put the nadir at 124.

24 MS ANYADIKE-DANES: Can I just ask you that, let's just say that

25   she did, Professor Young, because nobody knows what she got,

26   but let's just say that she did, and you have got the nadir at

27   124, did you say?

1   PROFESSOR YOUNG: Yes.

2   MS ANYADIKE-DANES: Is that a significant difference between 127

3   and 124?

4   PROFESSOR YOUNG: I mean I, so I think most people or frequently

5   people view 125 as kind of threshold and I think would have

6   done in that era.

7   MS ANYADIKE-DANES: Yes.

8   PROFESSOR YOUNG: So once it is below 1, I mean I think people have

9   commented that 127 they kind of didn't think was especially

10   abnormal.

11   MS ANYADIKE-DANES: Uh-huh.

12   PROFESSOR YOUNG: But I think once it's below 125 everybody would

13   have looked at it differently.

14   MS ANYADIKE-DANES: So in your view the figure that you would have

15   got based on the administration of 500 would have produced a

16   serum sodium level that you think pretty much everybody would

17   have recognised as being significant?

18   PROFESSOR YOUNG: Yes.

19   MS ANYADIKE-DANES: Okay. And on your 250 where are you, you're

20   about 126; is that right?

21   PROFESSOR YOUNG: 126.

22   MS ANYADIKE-DANES: Yes.

23   And then, Dr Haynes, if I turn to you now, you've got

24   slightly lower figures because you take a different view of

25   the way in which the body water would have, or at least the,

26   if I call it, is that the equilibrium point, can I call it

27   that?

1   DR HAYNES: Yes, the rate at which redistribution occurs around the

2   body.

3   MS ANYADIKE-DANES: Yes. And so you make more adjustments for that

4   and that produces slightly lower figures for you?

5   DR HAYNES: Yes, but even putting that to one side, if you, say,

6   used total body water you're still getting an answer that said

7   124, 125 --

8   MS ANYADIKE-DANES: And that is, do you regard that in distinction

9   to 127 as being a significant difference?

10   DR HAYNES: Yes. Because if you look at the magnitude of change

11   and say it drops from 137 to 127, that's a change of minus 10.

12   MS ANYADIKE-DANES: Uh-huh.

13   DR HAYNES: If it drops from 137 to 124, that is 13 of a drop.

14   MS ANYADIKE-DANES: Uh-huh.

15   DR HAYNES: Which is 30% alteration in the decrement, 30% of

16   anything is quite a lot.

17   MS ANYADIKE-DANES: Okay.

18   DR HAYNES: Can I, also let me add that if the serum sodium say,

19   for the sake of argument, that it had initially been 130.

20   MS ANYADIKE-DANES: Yes

21   DR HAYNES: And then came back as 120.

22   MS ANYADIKE-DANES: Yes

23   DR HAYNES: You've got the same rate of fall but subliminally I

24   think people might have paid more attention to that but it

25   would have no different acute consequence, the --

26   MS ANYADIKE-DANES: I see

27   DR HAYNES: -- 137 to 127.

1   MS ANYADIKE-DANES: And we've been taping this and we're going to

2   produce a transcript of this conversation which may assist

3   you, what I think is likely to assist the Chairman is if

4   perhaps having seen that the two of you can produce a joint

5   paper that will describe what the exercise that you're

6   embarking on was, what the complexities surrounding that are,

7   how you both approached it, and where you are now; does that

8   seem sensible?

9   DR HAYNES: Yes. Okay.

10   PROFESSOR YOUNG: Yes, I mean I'm sure that we could do that, yes.

11   MS ANYADIKE-DANES: In some respects you've already described that

12   in this transcript so I'm hoping that this transcript will

13   assist you in doing that.

14   DR HAYNES: Yes.

15   MS ANYADIKE-DANES: And then that can be --

16   PROFESSOR YOUNG: Yes, no, that's fine.

17   MS ANYADIKE-DANES: And then that can be circulated. I think also

18   your latter observations about, well even if we leave aside

19   the exercise that has troubled us for so long in doing and we

20   stick with 127 your latter observations of the significance of

21   that as a fall from 137 are also helpful.

22   DR HAYNES: Right, yes, I think so, yes.

23   PROFESSOR YOUNG: Yes, okay.

24   MS ANYADIKE-DANES: If in the course of doing that anybody comes up

25   with any other paper that you think will assist, because as

26   you know these documents are not just read of course by the

27   interested parties, and by the Chairman, they're there on the

1   website and they are read by others, so if there's any other

2   paper that you would wish to attach to an agreed position like

3   that then do let us know and we can arrange for that to be

4   attached.

5   PROFESSOR YOUNG: Thank you. I mean there is one other minor point

6   I want to make, and partly for my own interests with Dr

7   Haynes, and that relates to, I think, the discussion in the

8   mid 90s by Arief --

9   DR HAYNES: Yes.

10 PROFESSOR YOUNG: -- who was arguing that the rate of fall didn't

11   matter and was not related to the risk of cerebral oedema.

12 MS ANYADIKE-DANES: I think he said that the --

13 PROFESSOR YOUNG: Yes, if --

14 MS ANYADIKE-DANES: -- it wasn't well correlated, it might matter

15   but the correlation was not strong.

16 PROFESSOR YOUNG: No, and actually I did not agree with him in the

17   mid 90s, I should say.

18 MS ANYADIKE-DANES: Uh-huh.

19 PROFESSOR YOUNG: But I'm interested to know to what extent there

20   was awareness of his views on that among the paediatric

21   community.

22 DR HAYNES: Right. What is this, and it kind of taxed me through

23   every stage of my involvement with this, and it's trying to

24   look back and see. I mean I became a consultant here in 1994

25   and during the latter part of my training there was very much

26   an awareness that giving hypotonic fluids, as had been done

27   for years to children, for anything other than basic

1   maintenance needs was potentially hazardous. And it was only

2   really when Des Bohan and his group published from, it seems,

3   the BMJ that a lot of people sat up and looked and thought

4   seriously about it and then began to look back at what Arief

5   and company had produced. So I think around the country, and

6   it's a fairly small community, if you like, various pockets of

7   strong belief, if you like, began to spring up. And people

8   began to in individual areas develop kind of an evangelical

9   crusade against it or against indiscriminate use of hypotonic

10   fluid because of the potential for hyponatraemia.

11 MS ANYADIKE-DANES: But if you leave logic aside and go to where

12   Professor Young comes from yes, people might have begun to see

13   the risks involved in, as you describe it, the indiscriminate

14   use of low sodium fluids and the risks of that producing

15   hyponatraemia. But the rate of fall bit is actually quite a

16   specific issue because it deals with how quickly you develop

17   your hyponatraemia, which is one aspect that concerned people,

18   the other which is the one that Malcolm Coulthard in his work

19   for the Inquiry on Adam talked about, which is the rate of

20   correction, either way you're talking about the rate of

21   change. And what Dr Crean did when he attached to his third

22   witness statement in the Lucy case, the 1993 Arief paper and

23   the exchange between he and Simon Ellis at Radcliffe on that

24   was to point out that what might have been accepted which was

25   it was that rate of change, whether by correction or by

26   deterioration, that led to your, or contributed to the

27   development of the fatal cerebral oedema. That may not be

1   established clinically, that may be people's gut feeling it

2   must be so but what Arief was saying is well, actually if you

3   look at the evidence you don't have a strong correlation. And

4   I think that's, Dr Haynes, where Professor Young was coming

5   from which is whether you in your practice had any

6   appreciation of what your colleagues were thinking about that

7   type of argument. Sorry, have I got your point correctly,

8   Professor Young?

9 PROFESSOR YOUNG: Yes, yes, that is correct. I mean it was

10   something that I was aware of but I just felt it might be a

11   slightly esoteric debate and that there was a wider view that

12   the rate and magnitude of fall were the important things and I

13   was just trying to establish with Dr Haynes if he had had any

14   awareness of it or had heard it discussed, etc.

15 MS ANYADIKE-DANES: Yes. Can you help with us that?

16 DR HAYNES: It was discussed I think with increasing frequency and

17   I think there's a -- from probably about 1997 onwards, there's

18   a very significant awareness of the dangers of using hypotonic

19   fluids. And I've tried to find out when in this Trust we

20   stopped having available this normal saline and I think it was

21   round about 1997.

22 MS ANYADIKE-DANES: Yes. But if you go to the particular point

23   that Professor Young is asking is: Well, what about this issue

24   is the rate of change, let's call it that, the rate of change

25   well correlated to the development of cerebral damage or the

26   extent of cerebral damage.

27 DR HAYNES: I think the acknowledgment is based mostly on anecdotal

1   experience.

2 MS ANYADIKE-DANES: That it is well correlated?

3 DR HAYNES: Yes.

4 MS ANYADIKE-DANES: And does that mean --

5 DR HAYNES: If you use correlation you're implying a scientific

6   application.

7 MS ANYADIKE-DANES: Well I was thinking, what I think that

8   Professor Arief was saying is that he hasn't seen good

9   evidence on the clinical side that you can match up reliably a

10   rate of fall --

11 DR HAYNES: Yes, but if you --

12 MS ANYADIKE-DANES: -- to an extent of cerebral damage.

13 DR HAYNES: If you look at the paper that came from that he wrote I

14   think I said it in my first attempt to put a statement for

15   this question, that his statement comes from a little table in

16   which he's done a two by two either Fisher or Chi-squared look

17   at those who developed hyponatraemia over 24 hours or more

18   than - or over more than 24 hours.

19 MS ANYADIKE-DANES: Sorry, Professor Young, I don't know, do you

20   have that exchange, it was attached to the third paper of

21   Professor, of Dr Crean, and I can give you the reference for

22   it.

23 PROFESSOR YOUNG: Yes, well I'm familiar with the exchange between

24   Arief and, yes.

25 MS ANYADIKE-DANES: Yes.

26 PROFESSOR YOUNG: Yes, there was a letter exchange in the BMJ I

27   think on this.

1 DR HAYNES: Yes, that's right, yes.

2 MS ANYADIKE-DANES: That's right. And the reference to it for the

3   purposes of the Inquiry is 253002019.

4 PROFESSOR YOUNG: Yes, because that was I think the first time I

5   had really come across the idea that there was not a

6   relationship between the rate of fall and risk of cerebral

7   oedema. And, you know, I remember considering it at the time

8   and thinking that okay, Arief's probably wrong. But I was

9   just, I just didn't know to what extent that that discussion

10   had taken place in the paediatric community.

11 MS ANYADIKE-DANES: Yes. If we just give the particular part of it

12   that you are debating, if I can put it that way, is what Arief

13   says in response to Simon Ellis's point

14   *"Data showing that either the magnitude or the rate of*

15   *development of hyponatraemia correlates with brain damage do*

16   *not exist. On the contrary a recent prospective study of 739*

17   *patients who were hyponatraemic post-operatively clearly shows*

18   *that neither factor has any relation to brain damage*".

19   Now that's, if I can encapsulate his point, that's where it is

20   and all that Professor Young wants to know, Simon, is in your

21   community was there an awareness of that position?

22 DR HAYNES: That the velocity of change in terms of - yes, yes.

23   There was an awareness, I think particularly among the

24   neonatologists probably.

25 MS ANYADIKE-DANES: Amongst the who?

26 DR HAYNES: Particularly among the neonatologists.

27 MS ANYADIKE-DANES: Neonatologists.

1   DR HAYNES: That there was, that the rate of change was

2   significant.

3   MS ANYADIKE-DANES: No, he's saying the opposite. He's saying

4   exactly the opposite. He says: *"On the contrary the recent*

5   *prospective study"* --

6   DR HAYNES: But then if you follow up what he says in that

7   letter --

8   MS ANYADIKE-DANES: Yes.

9   DR HAYNES: -- with his own reference back to his own paper --

10   MS ANYADIKE-DANES: Yes?

11   DR HAYNES: -- he is basing what he says on something that's pretty

12   spurious.

13   MS ANYADIKE-DANES: No, no, no, this particular one he's basing on

14   his prospective study looked retrospectively at 739 patients.

15   That's what he's basing this on.

16   PROFESSOR YOUNG: Yes, so he had quite a large data set basically.

17   MS ANYADIKE-DANES: Yes.

18   DR HANYES: And he was saying actually no whenever I look at my

19   data there is no evidence that rate of fall or poor magnitude

20   of fall matter?

21   MS ANYADIKE-DANES: Exactly. I mean that's why I read that bit out

22   because it is eye catching:

23   *"On the contrary a recent prospective study of 739 patients*

24   *who were hyponatraemic post-operatively clearly shows that*

25   *neither factor has any relation to brain damage."*

26   PROFESSOR YOUNG: And it was my impression that that rather, it was

27   my impression that in that opinion was not widely discussed.

1   But that was my impression and I still don't think that that

2   view of Arief is widely discussed or has subsequently been

3   widely discussed, but that's why I was interested to know

4   because Dr Crean had attached it.

5   MS ANYADIKE-DANES: Exactly. So, Dr Haynes, the question for you

6   is were you aware of that or were your colleagues?

7   DR HAYNES: Of what Arief said in that statement?

8   MS ANYADIKE-DANES: Yes.

9   DR HAYNES: No, I think is the answer.

10 MS ANYADIKE-DANES: Or of that view?

11 DR HAYNES: Of that view, yes. The view was that the rate of

12   change was important --

13 MS ANYADIKE-DANES: No, I meant --

14 DR HAYNES: -- and using it to look at the rate of change.

15 MS ANYADIKE-DANES: -- the view that it might not be. I understand

16   that for some of you that, and this is part of the concern

17   that you had about the use of low sodium fluids, that the rate

18   of change might be relevant, in a way what Professor Arief is

19   doing is, I suppose, attacking the orthodoxy in suggesting you

20   might have all thought that but you thought that for anecdotal

21   reasons. If you actually look at some of the studies being

22   done that's not well demonstrated, as I understand his paper.

23 DR HAYNES: Yes, but -- sorry Ian.

24 PROFESSOR YOUNG: And that's also how I interpreted it. He was

25   saying actually no, the development of cerebral oedema is more

26   idiosyncratic, is effectively what he was arguing, although he

27   didn't use those words, he was saying --

 1   MS ANYADIKE-DANES: Yes.

 2   PROFESSOR YOUNG: -- it's not related to rate of fall, it's not

 3   related to magnitude of fall.

 4   MS ANYADIKE-DANES: Exactly. And of course that leaves the big

 5   question is well if it isn't then what should you be looking

 6   at in order to ascertain whether you've got a more or less

 7   vulnerable patient?

 8   PROFESSOR YOUNG: But it sounds to me as if in fact Simon in his

 9   community wasn't aware of that --

10   MS ANYADIKE-DANES: I think that might be --

11   PROFESSOR YOUNG: -- contrary view?

12   MS ANYADIKE-DANES: That seems to be the conclusion from what

13   you're saying, Simon, you weren't aware of that as being a

14   view?

15   DR HAYNES: No, there's an increasing gathering of the momentum of

16   the dangers of hypotonic fluids and allied with that the

17   danger of, for example, over rapidly correcting

18   hypernatraemia.

19   MS ANYADIKE-DANES: Yes, I don't think that Professor Arief is

20   saying that there aren't dangers associated with the use of

21   low sodium fluids. I think on the contrary he is saying that

22   there are --

23   DR HAYNES: Okay, yes, yes.

24   MS ANYADIKE-DANES: -- dangers but he is, this particular paper is

25   addressed to a very specific aspect.

26   DR HAYNES: Uh-huh.

27   MS ANYADIKE-DANES: And I think what you seem to be suggesting is

1   that you weren't particularly aware that he was attacking what

2   you might have regarded as an orthodoxy position. Would that

3   be fair, that you didn't appreciate --

4 DR HAYNES: I think he said that, yes.

5 MS ANYADIKE-DANES: -- he was saying that?

6 DR HAYNES: Yes, that's fair comment.

7 MS ANYADIKE-DANES: Yes.

8 DR HAYNES: And I'm trying to think back to 10/15 years ago and

9   it's, and it's certainly that his view which we talked about

10   just now certainly wasn't discussed in a particularly

11   widespread forum or given much time --

12 MS ANYADIKE-DANES: Yes.

13 DR HAYNES: -- in the paediatric intensive care community.

14 MS ANYADIKE-DANES: And does that mean because you weren't aware of

15   it that that was a view that he was holding and discussing?

16 DR HAYNES: Well from, I mean I would have to say for me personally

17   that the answer has to be yes.

18 MS ANYADIKE-DANES: Okay.

19 DR HAYNES: But I can't speak for anybody else.

20 MS ANYADIKE-DANES: Okay. Does that help, Professor Young?

21 PROFESSOR YOUNG: It does indeed help. No, I mean I was just

22   interested in it as a point, it's probably in keeping with my

23   impression and I'm actually not sure whether Dr Crean was

24   aware of that view or not in 2000, I mean obviously he is

25   aware of it now. But --

26 MS ANYADIKE-DANES: Do you know where matters stand now as a matter

27   of interest, Professor Young, with that --

1   PROFESSOR YOUNG: Sorry?

2   MS ANYADIKE-DANES: -- do you know where matters stand now with

3   that argument that Professor Arief was developing there?

4   PROFESSOR YOUNG: I mean I think the consensus today is that rate

5   of fall and magnitude of fall are important factors. But I do

6   think that Arief was getting at something which has validity

7   and it does come back to this question of idiosyncricity so

8   that, you know, it's not predictable whether an individual

9   will develop cerebral oedema based simply on the rate and

10   magnitude of the fall in serum sodium.

11   MS ANYADIKE-DANES: Yes, and are you aware of people researching

12   now to try and refine matters, if you like, it's not as simple

13   as a ready reckoner, well if you've got rate and magnitude of

14   fall that will do it. If it's not as simple as that, that's a

15   bit of a crude way of looking at the problem, are you aware

16   now of people trying to get to a more refined answer of why

17   some children do because they don't all develop hyponatraemia.

18   In the work that the Inquiry has done that's been part of the

19   problem and --

20   DR HAYNES: Yes.

21   MS ANYADIKE-DANES: -- and why the use, I presume the use of low

22   sodium fluids continued for so long because it worked

23   perfectly adequately for so many children?

24   DR HAYNES: Yes, but -- two separate things that you mixed up

25   there.

26   MS ANYADIKE-DANES: Sorry, what was that?

27   PROFESSOR YOUNG: So one is whether they develop hyponatraemia --

1   MS ANYADIKE-DANES: Yes.

2   PROFESSOR YOUNG: Or not?

3   MS ANYADIKE-DANES: Yes.

4   PROFESSOR YOUNG: -- following the administration of certain fluids

5   and, secondly, whether that hyponatraemia gives rise to

6   cerebral oedema or not?

7   MS ANYADIKE-DANES: I beg your pardon, yes, that's what we are

8   actually getting at is whether the hyponatraemia that they

9   develop contributes to the development of a cerebral oedema

10   which may prove fatal.

11   PROFESSOR YOUNG: Yes, I mean it --

12   MS ANYADIKE-DANES: That's a bit of it, it's not, you are quite

13   right, I was being a bit loose, I didn't mean just a

14   straightforward development of hyponatraemia.

15   PROFESSOR YOUNG: So I mean if I can comment on it.

16   MS ANYADIKE-DANES: Yes.

17   PROFESSOR YOUNG: I am aware of ongoing work, more focused actually

18   on the first part of your question why some individuals will

19   develop hyponatraemia.

20   MS ANYADIKE-DANES: Yes.

21   PROFESSOR YOUNG: And that ongoing work is looking at genetic

22   factors --

23   MS ANYADIKE-DANES: Okay.

24   PROFESSOR YOUNG: -- though variation in, for instance, sodium

25   pumps --

26   MS ANYADIKE-DANES: Yes.

27   PROFESSOR YOUNG: -- which help to control levels of sodium and

1   also variation in certain hormones, natriuretic peptides and

2   their receptors. So I think there are some genetic factors

3   which contribute in part to that variability in sodium

4   response.

5 MS ANYADIKE-DANES: And then the --

6 PROFESSOR YOUNG: -- that will receive fluids.

7 MS ANYADIKE-DANES: -- and then the relationship between the

8   hyponatraemia and a fatal cerebral oedema?

9 PROFESSOR YOUNG: So I am not aware of ongoing work to explain

10   that, there may be such work but I'm not aware of it.

11 MS ANYADIKE-DANES: I understand. And Dr Haynes?

12 DR HAYNES: No, I'm not aware of anything to look at why some

13   children or some patients develop cerebral oedema and others

14   don't for the same decrement in serum sodium.

15 MS ANYADIKE-DANES: And the expression that Professor Young has

16   used there 'idiosyncrasy', is that something that is gaining

17   some traction, some understanding that that does exist and

18   it's a relevant thing to consider?

19 DR HAYNES: Particularly, yes, particularly inappropriate ADH

20   response to illness and injury. There are children who

21   produce a very marked, or it appears to be a very marked ADH

22   effect, particularly in terms of respiratory illness.

23 MS ANYADIKE-DANES: And do people know why?

24 DR HAYNES: No, no one knows why. It's just something that you are

25   aware of, you may get two children with a viral pneumonia of

26   the same, leaving the same impact on the lungs, one of whom

27   will develop a surge of 120 with the same feeding and fluid

1   administration, the other will keep a sodium that's 135.

2 MS ANYADIKE-DANES: And if they're responding in that way

3   differently to the production of AD -- well, an SI ADH, I

4   suppose ultimately --

5 DR HAYNES: Yes.

6 MS ANYADIKE-DANES: -- then that affects their water retention and

7   that leads into some of these issues that we're discussing?

8 DR HAYNES: Yes.

9 MS ANYADIKE-DANES: Would you accept that, Professor Young?

10 PROFESSOR YOUNG: Yes. No, I mean I would, and I agree that

11   there's marked variation in response among individuals, I

12   think some of that has a genetic basis, as I suggested

13   previously, but there may well be other factors contributing

14   as well and that basically is an area that people are

15   researching.

16 MS ANYADIKE-DANES: Well thank you both very much indeed. From the

17   Inquiry's point of view, we're very grateful to you making the

18   time to discuss this. So we will get this to you just as soon

19   as we can and it would be very helpful if you could produce

20   something jointly because I think that would be most, of

21   greatest use to the Chairman.

22 DR HAYNES: Are you happy if we communicate directly with each

23   other while we formulate this?

24 MS ANYADIKE-DANES: Yes, yes. As long as, if that communication

25   should lead to any further development into your thinking on

26   that, that you keep a note of that so we know how matters have

27   developed from this conversation.

1   DR HAYNES: Right. So you'll send us both a transcript?

2   MS ANYADIKE-DANES: Yes.

3   DR HAYNES: And we will need to work out the best way of coming up

4   with a consensus view?

5   MS ANYADIKE-DANES: Yes.

6   DR HAYNES: And we'll agree it and send it to you?

7   MS ANYADIKE-DANES: That's right. But please, as I say, because

8   we're trying to make sure that all these things are

9   transparent if in the course of your conversation to ensure

10   that you have both got the agreed position you move on from

11   this, from this discussion, if you could record that because

12   people will be wanting to see what the differences are between

13   what you were discussing in here and what you produce.

14 PROFESSOR YOUNG: Okay.

15 MS ANYADIKE-DANES: Okay.

16 PROFESSOR YOUNG: I think that's, yes, that's absolutely fine, yes.

17 MS ANYADIKE-DANES: Thank you both very much indeed.

18 DR HAYNES: Ian, I'm just about to go on holiday for 10 days.

19 PROFESSOR YOUNG: Okay, Simon, so I think we'll be in communication

20   when you come back then, all right.

21 DR HAYNES: Yes. So if you want to send me anything I will pick it

22   up when I come back.

23 PROFESSOR YOUNG: Lovely. Okay.

24 DR HAYNES: But I'd be delighted to.

25 PROFESSOR YOUNG: And nice to talk to you, okay.

26 DR HAYNES: Well it's nice to meet you, so to speak.

27 PROFESSOR YOUNG: Right okay.

1   MS ANYADIKE-DANES: Thank you both very much.

2   PROFESSOR YOUNG: Okay.

3   MS ANYADIKE-DANES: Bye now.

4   PROFESSOR YOUNG: Bye.