Wednesday, 5 December 2012

(10.00 am)

(Delay in proceedings)

(11.10 am)

THE CHAIRMAN: Ms Anyadike-Danes?

MS ANYADIKE-DANES: Good morning. Dr Squier.

DR WANEY SQUIER (called)

Questions from MS ANYADIKE-DANES

MS ANYADIKE-DANES: Dr Squier, you were also instructed in the Adam Strain case; is that right?

A. Yes, that's correct.

Q. And you produced reports for that case and you also gave oral evidence in the course of that case.

A. I did.

Q. I have the transcript from your oral evidence. In fact, your CV was dealt with there. The date for the transcript is 12 June of this year. It starts at page 41, literally, but if we can pull up 42 as well. 42 deals with the reports that you provided for the inquiry and how you adopt them.

Then your curriculum vitae is dealt with at page 43, and you can see at the top your training and your background and where you work. I wonder if I could ask you in this way rather than to repeat matters that you've already given evidence about: are there any new

developments in the work that you do from when you gave your evidence in June?

A. I think the only new thing would perhaps be a new publication that's gone on to my publication list.

Q. Thank you. Can I ask you, because I'm not sure we did ask you that there, roughly how many children's brains -- babies' and children's brains -- would you see in the years?

A. I think over my career, the average is between 100 and 150 per year.

Q. Thank you. Would you, for example, know roughly how many you examined last year?

A. I don't know exactly, but I would think probably 100, 120, something like that.

Q. Thank you.

THE CHAIRMAN: Doctor, let me intervene. Since you gave evidence in June, an issue has been raised about whether you should in fact be retained by the inquiry as an expert at all and there has been considerable correspondence about that coming from the DLS on behalf of the Trust, my replies, your replies, and so on. In the course of that there's reference that you have been reported to the GMC as a result of the evidence that you gave and a finding by a judge or criticisms of you by a judge or judges in different cases. Right?

A. That's correct.

THE CHAIRMAN: When you last wrote to us, you indicated that the GMC had not imposed restrictions on your practice --

A. That's correct.

THE CHAIRMAN: -- which is an interim measure which they can take in serious cases pending the determination of a complaint.

A. That's correct.

THE CHAIRMAN: Since you wrote to us on that basis, what is the position with the complaint to the GMC about you?

A. There was a complaint made to the GMC on 1 April 2010. We have written to the GMC, who continue to make enquiries into this. Their position is they want to persist with their enquiries. They have not decided whether they're going to dismiss it or to bring it to some sort of conclusion.

THE CHAIRMAN: To your knowledge, since you indicated that position in correspondence, has the investigation of the complaint advanced?

A. Not as far as I'm aware. We have written to the GMC to ask them where they're going and what's happening, and they have said they've made no further progress.

THE CHAIRMAN: In two-and-a-half years?

A. It'll be three years on 1 April.

THE CHAIRMAN: Yes. Okay. The point which has been raised

is (a) that there has been criticism of you and (b) that the criticism in effect is that you can have a closed mind, which leads you not to take into account other interpretations of evidence or other explanations of events. That's the gist of the criticisms which have been made against you. Right?

In Adam's case, that has not been suggested by any party in the questioning in June, nor has it been suggested by any party who has made a submission to the inquiry. So that appears not to be an allegation which is made against you in the evidence that you gave in Adam's case to this inquiry. Right?

Whether the same point may be made against you in relation to the evidence you're going to give in Claire's case, we'll see in due course, and we'll see how far apart your evidence is from the evidence of Dr Herron and Dr Mirakhur and, indeed, for that matter, Professor Harding, who we are going to video link to this afternoon. So I'll consider that at that point. But I presume you accept that it is imperfect that there has been judicial criticism of you.

A. I accept it's very imperfect and I would very much like to deal with it, but I'm not in a position to do so.

THE CHAIRMAN: Because the cases in which you have been criticised are cases in the Family Court?

A. That's correct.
THE CHAIRMAN: And the evidence which is given in the Family Court cannot be discussed or publicised without leave of the Family Court judges?
A. That's correct and my lawyers at the Medical Protection Society have said I may not refer to them in any other way because we don't have the permission of the judges to discuss the contents of those hearings.
THE CHAIRMAN: If my understanding is correct -- and please tell me if this is wrong -- the criticisms all come from what are now called "shaken baby" cases?
A. Exactly.
THE CHAIRMAN: And you have said in your last letter that you were formerly a believer in one approach to them and, through your involvement in those cases, you have changed sides, to put it rather crudely.
A. That's correct, I read the evidence, which was said to support the hypothesis of shaken baby syndrome, and found it was really wanting and there was no good evidence to support that hypothesis. I now give evidence on the basis of what I see and what I believe from all of the published literature available, which is contrary to the mainstream view on shaken baby syndrome.
THE CHAIRMAN: Are you on your own in that?
A. No, not at all, not by any means. There are many people

around the world and in this country who support me. The difficulty is that many of the people who agree with me are unwilling to say so publicly.
THE CHAIRMAN: But do some say so in evidence which they give to the courts?
A. Some do, yes, and indeed in the last few months we've had people from the staunchly pro shaken baby hypothesis, the mainstream, one particular expert is now saying: well, we actually don't know, it's all informed speculation.
THE CHAIRMAN: I think you have referred to that in your last response, have you?
A. Yes, because I think it's important. I think it's showing that even the staunchest believers in shaken baby syndrome are recognising that the science just isn't stacking up to their viewpoint.
THE CHAIRMAN: For how long has this debate been ongoing among pathologists and then, through them, into the courts?
A. The whole hypothesis of baby-shaking was first of all presented in about 1970, and I think it was probably about 1996/1998 that the Louise Woodward case came up in the United States, which received huge publicity, when people started to really focus on it and concentrate their minds on it. In the United Kingdom,

a pathologist called Gillian(?) Geddes wrote a very important paper in 2001 where she pointed out some important pathological features of the brain injury in babies thought to have been shaken and saying these babies don't have in fact any traumatic injury; the majority have brain swelling due to the lack of oxygen supply, and I think that was a very important turning point. Certainly to me, that brought home to me the fact that the pathology was not stacking up and we had to re-think the whole hypothesis.
THE CHAIRMAN: Okay. I think a specific and direct criticism is that you did not raise this with me at the inquiry. That issue has been specifically addressed. Do you accept that, in fact, it is something that you should have indicated to me?
A. I was, first of all, recommended as an expert to the inquiry by Dr Marcovitch, who knows very well of my background and my views, and we've discussed it on many occasions.
THE CHAIRMAN: Dr Marcovitch is one of the inquiry's expert advisers.
A. Yes.
He is in a position to be well aware of what my views are and the kind of criticism I might have been subject to because of those views. Certainly, I was

aware that Ms Anyadike-Danes was also aware of my --
THE CHAIRMAN: And did you assume that because Dr Marcovitch knew of this controversy that that would reach me?
A. I assumed he wouldn't have recommended me if you thought there was a problem about my evidence and that it would have reached you in that way. It has also been made very public, so ...
THE CHAIRMAN: Okay. I'm going to continue with the evidence. There was an indication from DLS in correspondence that it was considering judicial review of the fact that Dr Squier was going to give evidence. That was in correspondence some time ago and I will accept Dr Squier giving evidence for the reasons which have been set out in the correspondence.
Ms Anyadike-Danes.
MS ANYADIKE-DANES: You have produced reports on Claire's case also for the inquiry.
A. Yes, I have.
Q. Just for reference purposes, the series number of those reports is 236. I think you produced your first report, dated 16 June 2012. Then you produced a supplemental report, which is dated 18 June 2012, and that supplemental report started off and, in large part, dealt with the analysis of tissues and slides, and we can go into that a little bit for you to help us with

your interpretation of that.

Then you produced a further report on 22 August 2012, which was a supplemental report referred to as an addendum. In that, you were dealing with, again, the slides, on this occasion the slides you received, which had been reviewed by Dr Harding, which were in turn the slides originally provided by the pathologists, Dr Herron and Dr Mirakhur. And that report was in large part addressing -- and you also brought in, if I can put it that way, Dr Philip Anslow to look at the CT scans and provide a report to you to assist with that. His report is dated 24 August 2012.

Then you produced your final report for the inquiry, which is dated 5 November 2012. That report deals with a number of matters, matters more to do with the conduct, if I can put it that way, of brain-only autopsies. It goes into a little more detail about the evidence that you found and attaches some of your own slides and images to assist with explaining your views and why they differ from those of Doctors Herron and Mirakhur. And you also addressed some of the criticisms -- or the differences, if I can put it that way -- that Doctors Herron and Mirakhur have sought to make between the views that you have expressed in your report and those that Professor Harding expressed in his

report to the PSNI and also his very short report to the inquiry.

A. Yes.

Q. Do you adopt those reports, subject to anything that you might say now in your oral evidence?

A. Yes.

Q. Thank you. Have you had an opportunity, prior to today, not only to look at the witness statements of Dr Mirakhur and Dr Herron, but also to look at the transcripts of their evidence?

A. Yes, I have.

Q. Thank you very much. And you have seen the reports of Professor Harding?

A. Yes, I have.

Q. Thank you very much. I wonder if I could ask you firstly a little bit about protocols and guidance. It features in your reports in two places, but I think your most recent report is perhaps the most comprehensive in terms of attachments. You have provided for the inquiry a number of guidelines and protocols in addition to articles and your images. So I want to ask you a little bit about the protocols and guidance.

The first is the 1991 joint working party on autopsy and audit. I'm just going to list out the ones and then ask you their significance so far as you can help us

with that. You also refer to the 1993 Royal College of Pathologists guidelines for post-mortem reports and the practice guidelines for necropsy. You may not have referred to that, but I'll ask you if you're aware of it. Then the guidelines on autopsy practice, 2002, which are the updated ones from the 1993 guidance.

So far as you can help us, what is the role that those guidelines provide to a pathologist?

A. I think the guidelines are there in order that pathologists know what the fundamental requirements or recommendations are for their practice. I have to say that my own experience is that, in 1996, we weren't as concerned with knowing about them and understanding them as we are today. Things have changed tremendously since 2000 in terms of our requirement for guidelines, our reference to guidelines, the numbers of guidelines that we have, and indeed I think in the whole area of our practice, which I think is the same in every profession now, the far closer management and accredibility and accountability that we all have.

In 1996, I think these guidelines were there so there was an understanding of the basic practice that was expected to be adhered to or the basic recommended practice for pathologists at that time.

Q. And so far as you are aware, were those guidelines

materials that pathologists recognised, accepted were there and maybe adapted to their own local needs?

A. I think very much so. I think at that time departments functioned along their own particular ways. Their own traditional way of practising would have been probably more common than adapting to published guidelines.

Q. And so far as that didn't compromise the main objective that was the concern identified in the particular guideline, that just carried on?

A. Yes. I think so.

Q. You mentioned in 2000, but prior to 2000 was it a practice that audits were done of autopsies so that one was able to keep abreast of how many were being conducted, what their turnaround time was, that sort of thing?

A. I think this may have been done on a very informal basis in most departments, yes.

Q. You may not be in a position to answer other than in your own practice, but so far as you are aware is there greater or lesser demand now to have autopsies? You would see them as brain-only autopsies because that's what you would typically be involved in. Do you do more now than in 1996?

A. More brain-only autopsies?

Q. Yes.

A. I don't think in the general run of practice they are more frequent than they were. In my own environment, it certainly is far more common because a lot of my colleagues are doing work on brain diseases which simply require the brain that's been donated for research to be taken. But I think in the general run of diagnostic neuropathology, when an autopsy is being done in order to establish a diagnosis, that the most frequent autopsy would be a complete, whole-body autopsy.

Q. But if there were to be any increase in demand, if I can put it that way, for the involvement of a pathologist, is that coming more through research than diagnostics?

A. In my own department, the increase in demand is coming through research because the numbers of post-mortems done generally has dropped hugely over the last couple of decades. And in fact, most post-mortems are now done at the request of the coroner rather than for hospital diagnostic or medical interest purposes.

Q. So the sort of autopsy that was done in relation to Claire, which is a hospital autopsy by consent for diagnostic or maybe potentially some learning benefit, that kind of autopsy is on the wane?

A. Yes.

Q. I wonder if I can ask you this question too, which is in relation to the starting materials, if I can put it

that way that the pathologist has before they commence the autopsy.

The evidence has been from Dr Herron and Dr Mirakhur that you have the autopsy request form, which you either may have physically with you, or you might have a conversation about it, but at some stage you will have that information, and also the consent form for the type of autopsy that was done on Claire. And you may or may not have the medical notes and records and the charts.

A. Yes.

Q. In your experience, how important are the medical notes and records?

A. It's very important that you have a good understanding of what it is that you're looking for an autopsy because you're doing a technique where you only have that opportunity to make certain observations. Once the autopsy is over, tissues will be lost, so there'll be no opportunity to go back to revisit certain aspects. I think one of the practical aspects, which I don't think was mentioned at all in the transcripts as I've read them --

Q. Sorry, just to be clear, when you say "tissue would be lost", you don't mean because, after you have studied the tissue, very often the tissue is not retained; do you mean the process of obtaining the tissue may itself

mean you have gone past other material that you could have saved and could have studied?

A. Yes, that's one particular aspect. For example, CSF was taken at autopsy. If you don't take it early on in the procedure either by putting a needle in the back of the head prior to opening the head or by putting a needle into the ventricles, as I think Dr Herron explained, there will be contamination with blood once you have opened and cut blood vessels. The other important feature is one should look at the skull and the various channels that the blood flows inside the skull at the time of autopsy because one won't be retaining the skull. So as far as a neuropathologist is concerned, that's very important information that one must obtain at the time because the body will then not be retained, that will be going off for ...

Q. When you say it's very important that you are given information which guides you as to what you should be looking for, is that because there are certain examinations which you wouldn't do unless you were alerted to a particular problem?

A. That's correct. Many of our autopsy techniques will be a sort of catch-all, will enable us to look for a variety of things we're not necessarily thinking about at the time, but there are certain things that we would

need to be previously aware of so that we make sure that we look for those things at the time of the autopsy.

Q. So then if I come back to your point, which is you need to be very clear about what the things are that you're looking for or might be considering, how do you get that level of clarity?

A. The ideal way is to talk to the clinicians who are involved. I've seen that there has been discussion about going through the case notes. One of the practical difficulties is that in every department that I've worked in, autopsies are usually done in the morning. Our autopsy staff come in very early and they want to be clear and finish by lunchtime and to finish off all the work. So one is often under some pressure to get in and get going and if the notes are only brought to you at the time, it may be that one has a pile of case notes that are very voluminous, that have been written in by many different people with different sorts of handwriting that can be incredibly difficult to read. One may be reading notes of a very junior doctor who has got up in the middle of the night and scribbled something which won't necessarily reflect the general impression of the case. So the best overall interpretation is to talk to the clinicians who will say what they really were concerned about is. And they will

give you a summary of the chief problems.

Those problems would, one hopes, be distilled into a request form where they're set out for the pathologist who can then look at one page, see what's required, if necessary look up certain details in the notes, but it's quite difficult to go through the notes and make sense of them prior to doing an autopsy, especially if they've only arrived at the time of the autopsy and you haven't had them the day before.

Q. And you don't have the guidance of what the clinicians have put in the autopsy request form or, for that matter, the clinician's view.

Does that mean you do look at the notes, but you look at them in the context of having either a discussion with the clinician or having had an opportunity to consider the autopsy request form?

A. Yes, that's right.

THE CHAIRMAN: If you're trying to do most of your autopsies in the morning and that's typically one of the busy time for doctors who are coming in, they're doing ward rounds, they're catching up with new admissions overnight and so on, that presumably increases the difficulty in actually getting to speak to the clinicians at the right time, does it?

A. That's true if it's just in the morning, but usually one

has notification that a patient has died and that an autopsy will be forthcoming. So it may be in the previous days one can talk to the clinicians, but often the notes aren't made available; they may go straight down to the autopsy suite with the body, so one won't have a chance to read them independently.

THE CHAIRMAN: But can I take it there are many circumstances in which, between your workload and the clinician's workload, this preferred way forward cannot be achieved?

A. I think that's correct, yes.

MS ANYADIKE-DANES: I had interrupted you when you were giving an answer, when you said that "a practical aspect that was not in the transcripts" -- and I wondered if I could invite you to go back. I can show you where it is in the note just to indicate to you.

A. I think that was it. I wanted to explain that quite often the situation is you hear there's going to be an autopsy, you go to the autopsy room in the morning, there's a pile of notes like this (indicating), and a group of technicians saying, "Come on, doc, we have got seven to do this morning, could we get on with it?". So sometimes there's quite a lot of pressure for you to get on with the autopsy and going through a lot of things can be difficult.

Q. So we'll come to it a little bit later on, but do I take it that if you haven't had an opportunity to discuss matters with the clinicians then, literally as you are about to start, because you're involved in brain-only autopsies typically, or at least that's the part of the autopsy that you'd be brought in to address, the brain is fixed for a period of time, do you ever consider it to be appropriate in that period of time between when you have taken the brain out and it is fixing for the four, six weeks, however long that might be, take an opportunity at that stage to discuss matters with the clinician?

A. Oh yes, one certainly would, and I would always invite the clinicians to comment and be present when we look at the fixed brain. The importance is that those features which we can only look at at autopsy need to be clear so that we don't miss things at that time.

Q. Yes. Then can I ask you about the limitation in Claire's case of the autopsy to brain-only. You in your report had referred to the fact -- and I can give you the reference to it. It's 236-007-006. You talk about the case of a child who has died suddenly with no clear clinical diagnosis, not only would you expect a full autopsy, but you'd expect a paediatric pathologist to be consulted or involved.

If you leave aside the aspect of a paediatric pathologist and concentrate on that fact that you would expect a full autopsy, why in your experience would you expect a full autopsy in those circumstances?

A. The only circumstances under which I would perform a brain-only autopsy is where that is all that we have been given consent for and the family have said they want as little to be done as possible. In every other circumstance, I would expect to do a full autopsy.

Q. So does that mean that the norm is the full autopsy and then there are circumstances in which the families don't wish that to be happening and when it's a consent-only, then you abide because you have no option by the family's consent?

A. Yes.

Q. Do you ever have discussions prior to the consent of the families being taken as to what should be the scope of the autopsy?

A. Yes, indeed. The clinicians I work with almost always inform me before an autopsy, almost always inform me. In fact, if they expect a child to be dying, they will talk to me about it and say, "We have a patient on the ward and we're very concerned that this patient may not survive and we will be wanting an autopsy", and they warn me to be sure that I will be there and that we

retain all the various materials that we need to to make the full diagnosis.

THE CHAIRMAN: When you talk about what the norm is, are we still talking about 1996 or are we talking about now?

A. I think in 1996, even more so, because we did more autopsies then and a full autopsy would have been the rule rather than the exception.

MS ANYADIKE-DANES: And if the indication to you is the family actually would prefer a more restricted autopsy, do you ever engage or involve yourself in a discussion with the clinician as to the potential benefits for doing a fuller autopsy or do you acknowledge, "That's the indications from the family and let's get on with it"?

A. If the indications are that the clinicians have had a full discussion with the family and that is the family's request, I don't challenge it because that's what the families want. I do get involved very frequently in the discussion about whether we can keep the whole brain or not, because that's something that's obviously very close to my own practice. And on a regular basis, I will either speak to families or offer to speak to families in order to help to inform them about the benefits of keeping the brain entirely.

Q. But in this case, what Dr Herron and Dr Mirakhur would

have received was the consent form signed by Claire's father, which made it very clear -- in fact, I think it was underlined "brain only". And if you received that, you wouldn't take the matter any further forward, I understand it?

A. No, I would assume the clinicians had sought appropriate consent and that's the consent that came back.

Q. It may not be entirely your area because you're a neuropathologist, but you have expressed the view that when you have a systemic infection that was suspected, as Claire's illness was on admission, then you wonder whether the brain-only was appropriate. In Claire's situation -- which of course you don't know until you have started it -- but what is it that you anticipate might have been the benefit of carrying out a full autopsy?

A. Well, the question of infection was one that was clinically uncertain and I think one needs to look to see if there's an infection that maybe was unexpected. She may have had infection elsewhere in the body that hadn't been diagnosed clinically and one doesn't know until one looks.

Q. But would it not have found its way to have some sort of evidence of it in the brain?

A. It may have done, but it may be that the brain was

reacting to an infection somewhere else in the body as well.

Q. So is it possible to have an infection somewhere else, the evidence of which has not reached the brain, but which can trigger something that ultimately leads to the cerebral oedema? Is that, as far as you are aware, possible?

A. Yes, that's possible, and I think particularly in a child such as Claire who had a history of epilepsy, the brain might have been vulnerable, so one could see a pathway for infection triggering seizures and seizures triggering brain swelling and so on and it is one of the pathways that one would want to explore.

Q. Even though you don't see the evidence of the infection itself in the brain --

A. Yes, indeed.

Q. -- the cerebral oedema having been the product of the seizures may be the result of it?

A. Yes, and even without seizures in between, some children will die very rapidly from an infection, for which there's very little evidence, except from post-mortem cultures or blood sampling.

Q. Apart from the slides that were made from the areas that were made, would you have expected or would it have been appropriate for any brain matter to have been taken for

the purpose of culture, perhaps?

A. I think in a case such as this, and perhaps almost routinely, one would want to keep a little piece of frozen brain tissue for the potential for culturing cells to look for DNA, for example, and a sample of tissue to be sent to the microbiology laboratories to be cultured for viral or bacterial infections.

Q. Both Dr Herron and Dr Mirakhur were asked that. Dr Herron's view was actually there was some brain material in the cerebrospinal fluid, so to that extent there had been some culturing, if I can put it that way, of the brain material. If we stop with that point, is that the sort of thing you mean, would that have yielded the sort of results that you're talking about?

A. I think it probably would have done, but I think normally one would expect both CSF and brain tissue to be sent because I think they would do slightly different tests. But it's quite possible and I don't know what the protocol was in the microbiology department here. It might be that CSF was to look for cells and to count the cells in it, but I think they probably also cultured it to look for the growth of viruses and bacteria.

Q. And Herron says that brain cells don't really culture, so maybe that was my incorrect terminology.

A. Yes, I think that's a different matter. The cells that

one would culture would be to look for -- there are two sorts of culture. There are cells that one cultures simply to look for DNA and you could do that from skin cells, for example. So a frozen sample might be kept either to look for culture at some point or to extract DNA from them, but the other sort of culture is where we take an example of tissue or some CSF and we put it on an agar dish and we put it in an incubator and we see what bugs will grow from it. So that's to culture the organisms which might be responsible for an infection.

Q. So it's not the brain, it's what you are looking for as any of the bacterial organisms that would have produced the evidence of the encephalitis, for example?

A. Yes, exactly.

Q. Thank you. You say that that's something that you do; is that something that is routinely done?

A. I think it's pretty routine, yes, especially if there's a question of an infection. I was just of course recalling that Dr Herron said he did this post-mortem in a special safety room.

Q. Suited up, I think.

A. Yes. So he was clearly aware of the risk of infection, so one would think all possible avenues would have been pursued to look for the infectious agent.

Q. And he described there to be certain limitations on

maybe how long he might spend looking at things because he was conscious that an infectious agent, as you called it, had not been ruled out, and so he was treating that case and possibly applying the local protocols for how you would deal with a highly-infectious situation.

Do you accept or is there some comment that you can provide for what are the constraints that that imposes on you if you think that's the environment that you have to work in?

A. Well, it's a difficult one because there are those who say: we're in a dangerous environment, we should have as little fresh tissue around as possible. So if one were looking at, for example, a Jakob-Creutzfeldt disease, where we know there is a prion disease which is very difficult to control, one would not take any fresh tissue for sending off to a laboratory at all. Everything would have to be kept in formalin and decontaminated.

In this case, I don't think this was ever a consideration and the infectious agents that one would have been looking for would have been relatively less harmful and relatively more easy to destroy in the environment by sterilisation.

Q. But how do you know that until you've actually examined the material? How do you know that it's safe to regard

it as fairly low level, if I can put it that way?

A. In this time I think that a child presenting in the way that Claire presented wouldn't have been considered to be a Jakob-Creutzfeldt disease, for example, so it would be based on the clinical history and a clinical suspicion that that is a possible disease and then one takes very special precautions. But you're absolutely right and, in fact, all our procedures should be such that we are safe whatever we're dealing with.

Q. I didn't particularly mean that disorder, but Dr Herron was in the position of not knowing what the viral agent might be, so he erred on the side of caution. That would be appropriate, wouldn't it?

A. It certainly would be appropriate, but I think it would also be appropriate that tissues should be sent for culture to look for the organism, which is what he did when he sent the CSF to the laboratory.

Q. The other thing you could be doing at that time is taking photographs and, in fact, there were no photographs taken of the whole brain. Do you have a view as to how appropriate it is to take photographs?

A. Again, it may be difficult to take photographs at the autopsy in a safe environment as there isn't always a camera handy. Particularly in 1996, it may be that there wasn't a set-up there to take photographs and

people wouldn't want a camera being brought into a safe room.

The question of taking photographs after the brain is fixed is quite different. By then we regard the brain as having been decontaminated in most circumstances --

Q. Safe?

A. -- so it's safe to handle and it would certainly be appropriate to take photographs.

Q. Apart from being appropriate, is it helpful to do that?

A. Extremely helpful because, in this case for example, there were no photographs taken of the whole brain and the question of whether there was coning -- in other words, the back part of the brain, the cerebellum, had actually been damaged and pushed through the foramen magnum at the back of the skull -- is an important question, how severe was the brain swelling, and we don't have any photographs to indicate that.

Q. When I asked Dr Herron about that, he said -- well, he actually described the brain, so if you're going to have a description of the brain, then it becomes just a matter of personal judgment whether you think over and above that it's helpful to have photographs.
Do you have a view about that?

A. I think photographs are extremely helpful and they save

a lot of difficulty with using long technical terms and description. But again, today we have very easily used digital cameras. In 1996 it was far more of a difficult procedure to take photographs and keep them because we were probably still using film cameras.

Q. When you say particularly when you have coning it's useful to have photographs, did you not know that you had coning from the CT scan, and if you knew that, what further benefit would be gained from having photographs?

A. I think it's always important to correlate the imaging on the CT scan with what we find from pathology -- we all learn from that, including the radiologists. We did know there was coning because the examination of the upper spinal cord showed a little bit of cerebellum to be displaced around the cord. That's a marker of coning. But I think it's always good to have all the information that we can have.

Q. It's one of those things and you're speaking about it in the negative because you didn't have it, but given what Dr Anslow described in his report in relation to the radiology and the CT scan, and given what you see in the autopsy report as to how the brain is described, would you have been assisted by seeing actual photographs of the brain, and if so, what is it that you are hoping to see or not see, which assists?

A. In a case such as this where there's brain swelling, we would hope to see the undersurface of the brain where the cerebellum comes into contact with the brainstem, which is where coning takes place, which is what actually is the fatal last process of brain swelling, and I think it would help us just too really understand how swollen the brain was and to go back and compare it with the CT scans and to be sure that we're looking at the same thing.

Q. And if you understand at that site how swollen the brain was or maybe have a better appreciation of the distribution of the swelling over the brain, what does that tell you in terms of what your report is seeking to do?

A. What it does is to confirm that the brain was swelling, to confirm that the brain swelling itself was likely to have been the cause of death because we have compression of the vital centres in the brainstem by the swelling. It may help us to understand the distribution of swelling through the brain, whether it was uniform throughout the brain or if some parts were more swollen than others. I don't think that helps terribly in making the diagnosis, but it's just of interest to note that.

Q. So it's of interest, maybe a learning point, but it

didn't advance matters further for the clinicians or the family if you know what the distribution of the swelling is?

A. No, I think the important thing is to say we can demonstrate that we have brain swelling, which has been the cause of death, and this correlates with what was seen on the brain scans.

Q. So that I'm clear about it, is it possible to have significant cerebral oedema, which is as seen in the CT scan, and yet find that ultimately that hasn't been the reason why the child died and that that's what you can see from photographs as opposed to any other evidence?

A. I think one can have brain swilling which isn't necessarily fatal. Brain swelling that can come and be resolved. But in a patient who has died, it is helpful to know that that was compressing those vital parts of the brain and was the cause of death.

Q. Thank you.

THE CHAIRMAN: Sorry, are these photographs more helpful for people coming along afterwards, like yourself, than they are for Dr Herron conducting the autopsy at the time? Because he can see the swelling, can't he, if there has been swelling?

A. Yes.

THE CHAIRMAN: So in 1996, it would never have been envisaged that Claire's death and the fallout from it would ever be the source of this inquiry. But even if it had been viewed at that time as being something which was likely to be reviewed at an inquest, Dr Herron would have been able to describe and refer to his findings on the examination of the tissue without having to have photographs?

A. He certainly could have done, yes, indeed.

THE CHAIRMAN: So the photographs might be an added extra or a bonus, but they're not essential to Dr Herron to do his job as a pathologist?

A. No, not at all. Just better for communicating his findings to other people.

THE CHAIRMAN: Right.

MS ANYADIKE-DANES: On that point, if one pulls up Dr Anslow's report, which is at 236-006-002. He's asked about the extent of swelling. He has examined the CT scan and he tries to describe what the extent of swelling is and does it by virtue of talking about whether there's descent of the cerebellar tonsils through the foramen magnum and so on. He's able to answer to 3, 4, 5, 6 and 7 to the positive, and then he is not able to answer the first point that you were saying that it might be helpful to have a photograph to

show because he says there's poor radiographic technique. Is that the sort of point that you hope would be clarified by a photograph?

A. Yes, exactly. It would obviously be available in the written report if it were described in words, but the photograph is just more helpful in conveying that.

Q. And to follow on from the chairman's question to you, because the prime purpose of this report was because the clinicians, at least so far as the family understood it, wanted it because they wanted to see certain features, for example the suspected viral encephalitis, and how that had actually contributed to her death. Firstly, was it present at all? It was suspected, and if it was, how it contributed to her death. And from Dr Steen's point of view, although there's a difference of view between her and the family about it, she also wanted to see if there was anything that might help explain Claire's developmental delay.

So those were the diagnostic purposes and other explanations that it was hoped that the autopsy could assist with. From the chairman's question to you, is there any other purpose from the report? Does it really matter whether people coming afterwards are able to interpret your logic and your thinking and so forth so long as the people who it was being provided to have had

their questions answered?

A. The primary purpose of a post-mortem and of writing a report at all is to inform the clinicians so that they can inform the family.

Q. And whether or not it's expressed in a way that those coming after you can clearly see your reasoning, how relevant is that?

A. Well, it's not the immediate, primary purpose of a post-mortem, which is to make a diagnosis and convey that to the family, but of course it's terribly important for teaching, and if there are photographs that makes it much easier to convey that information to others coming afterwards, who may want just simply to use it as a learning exercise.

But one has to, I think, add the caveat that I think we use photography very widely now because it's so easily available. In 1996, it might have been more difficult.

Q. Yes. And from the learning point of view, if the practice is that you present cases of interest, whether you call them neurological grand rounds, whether you call them multi disciplinary meetings, if you typically present them and engage in clinical debate or questioning about them, does that purpose make it important that the argument at least should be clearly

expressed and evidenced?

A. Yes, indeed, it does.

Q. If I go then to some of the specific elements, for example, the status epilepticus. I put to Dr Herron and Dr Mirakhur that the Royal College of Pathologists guidelines on autopsy practice in 2002 said that -- it wasn't written as if they were writing something that was novel at that time -- status epilepticus must be clinically documented. The reference for this is 314-008-062:

"Status epilepticus is a specific clinical entity and cannot be assumed from a post-mortem examination in the absence of good clinical documentation."

Is that something that you were aware of? Sorry, in 1996.

A. I think that's correct. I think, in 1996, nobody would have expected to make a diagnosis of status epilepticus from a post-mortem.

Q. From a post-mortem?

A. Yes. You wouldn't have dreamt of doing that.

Q. Would you expect to be told the source of the evidence in support of that diagnosis if you were carrying out a post-mortem in relation to a child where it is said that status epilepticus was one of the clinical problems?

A. One would trust one's clinical colleagues, if they're telling you that it was present, or they thought it was present, one would assume they had made that diagnosis.

Q. Would you expect to see any evidence of the EEG or how they'd reached that?

A. I would certainly trust my colleagues to give me that evidence and to rely on the evidence that they had given. I wouldn't be able to interpret an EEG, so if there were one, I wouldn't know if they had interpreted it correctly or not.

THE CHAIRMAN: So if there's a diagnosis of status epilepticus in Claire's case, it doesn't come from the pathologists, it has to come from the clinicians?

A. It does indeed, yes.

MS ANYADIKE-DANES: Thank you.

In the autopsy request form that went to the pathologists -- if I just pull this up for you because it's probably easier to see it in this way. If we pull up 090-054-183 and 184 alongside it.

You can see at the top right-hand side there's identified there four clinical problems, identified in order of importance: the first one is cerebral oedema; the second is status epilepticus; the third is inappropriate ADH secretion; the fourth is "query viral

encephalitis".

If one looks down to the bottom of the left-hand page, you can see what the clinical diagnosis was:

"Cerebral oedema, secondary to status epilepticus [and then] query underlying encephalitis."

The pathologists have taken the view that, brain only, they will obviously look at the brain in the round, so whether it says, "Please look and see the source of that mental handicap", they would obviously be looking for that, any sort of structural problem or lesion or something of that sort. But they would be looking to see the evidence, if there was any, so far as they could do it, of those clinical problems. And in the course of which, Dr Mirakhur said, well, she didn't think that there was very much they could do from the autopsy to assist with the second problem, status epilepticus, or, for that matter, the third problem, inappropriate ADH secretion. She thought they were essentially clinical matters.

If you received an autopsy request form with those sorts of problems, what is your attitude to how you go about dealing with them, if I can put it that way? Let's take the status epilepticus.

A. Okay. There are a few reports of specific brain pathology in status epilepticus. There are certain

cells which might be more prone to die in this situation, usually after very severe and very prolonged seizure activity. One wouldn't normally expect to see it because if there are other things going on, if there's brain swelling, if there has been restriction of oxygen supply to the brain, that might overarch the whole thing and cover any specific finding.

Q. You mean mask any of that evidence of cells that might have died as a result of that or be deranged as a result of that?

A. Yes. There would be an overwhelming pathology that would affect many areas of the brain and the specific subtle changes of status epilepticus would not be any longer obvious. I think the more important point is: why would a child of 9 years old have status epilepticus in the first place? That is where the antennae would be going up saying: there is something here that makes this brain more vulnerable to seizures, more likely to seize. Many 9 year-old children have all sorts of metabolic disruptions and so on and don't go in to uncontrolled seizures, even if they're non-fitting seizures as in status epilepticus.

Q. Part of the information that you would have received, if you were in the situation of the pathologists, is under that "past medical history", you see it there -- apart

from "mental handicap" it says:

"Seizures from six months to four years."

A. Yes.

Q. If you had got that bit of information along with the clinical problem of status epilepticus, what do you do with that as you conduct your autopsy?

A. One would look very carefully to see if there's any evidence of a structural abnormality in the brain that would be likely to predispose to epilepsy.

Q. Was does that mean exactly?

A. Looking for cells that are not properly formed, parts of the brain that are not properly formed, malformations or even early acquired damage that was there clearly before the first months of life, which gave an increased vulnerability to seizures.

Q. The evidence of those seizures, might you be looking for that?

A. Yes, there may be some secondary effect of seizures because we know that seizures specifically damage certain parts of the brain, particularly the hippocampus. So one would be looking for that, but also in the knowledge that there are many forms of epilepsy, which do not have any structural change, so the cause is not structurally identifiable. These are epilepsies caused by metabolic or electrical disruption of the

cells of the brain and we don't see that by microscopy.

Q. So you would be looking to see if you can see the evidence of something that might have predisposed her to the status epilepticus, even though you might not be able to see the evidence of the status epilepticus itself?

A. That's correct.

Q. In order to do that, what stains do you apply to your slides to help you see if you have the evidence of that antecedent experience, if I can put it that way?

A. Well, initially I think all pathologists do the same thing initially, which is to do what's called a haematoxylin and eosin stain. It's a basic stain which we just grow up with and we understand what sort of cells that's showing us, and it shows us the basic structures.

Q. Is that the H&E that's been referred to?

A. Yes.

Q. If you did the H&E, could that in and of itself show the sort of thing that you are looking for and therefore you don't need to do any more?

A. It may do, and if it does, then you would perhaps be happy and say: right, we've found something that would explain this child's predisposition to seizures. It may be that one would want to look further and say: well,

that gives us a hint, but we could look a little bit further and we could look for more evidence of malformation, but we could also look for evidence that those seizures had occurred and caused some scarring because we're well aware that in epilepsy something may trigger seizures, the seizures damage parts of the brain, and that sets up a vicious cycle. So those damaged areas of the brain start reacting to the damage and that seems to set up other cycles of seizure activity. So it's important to look to see if there's scarring in those very sensitive areas of the brain and specifically I mean parts of the hippocampus to see whether there might have been something going on there which would give us a clue as to this.

Q. If you don't see any traces of this sort of thing having applied your H&E stains, because you're looking to see if there's a link between her past history and the observed status epilepticus, could it be that if you applied the further staining that you're talking about, that what was not evident with the H&E, you begin to see the traces of with different stains?

A. It could be, that's why we do the extra stains. If we don't look, we're not going to find things. So we have a range of stains available to us that were also available in 1996, and it would be very simple just to

take that extra step. We may see nothing, but we may also get some extra information.

Q. And you've looked at the stains that Professor Harding looked at, which are also the slides that Doctors Herron and Mirakhur provided. When you just looked at those slides, did you see any evidence of the kind of thing that you're talking about?

A. I saw some very minor changes in the hippocampus, what's called dentate dispersion, where the cells, instead of forming a nice, neat band, tend to be a little bit ragged, but it was very subtle and it was not something that I would have based a diagnosis on on its own.

Q. And what does that mean, that ragged presentation?

A. It's something that's associated with epilepsy.

Q. So you say it's not anything that you would base a diagnosis on?

A. It was too subtle for that.

Q. So if you have something that in your view is not conclusive where does that take you?

A. Do some more stains and see if we can get any more information.

Q. What does the staining process actually do?

A. We use special stains to look for different cell types, so we can look for cells which are the normal cells of the brain, we can distinguish the nerve cells from, say,

the astrocytes, which are the cells that support and nourish the nerve cells, and they're also the cells that are responsible for causing scarring in the brain. So we would look to see if they're there, if there are too many of them, if they look as if they're reacting and causing scarring. We can also look at a whole range of different cell types, both endemic -- part of the inherent population of the brain -- or cells which have infiltrated from the brain from the blood. So we have a whole range of special stains and we just tailor-make a panel of stains according to the pathology that we're seeking to establish.

Q. I would assume from the way you've discussed it that the process of staining has become more sophisticated as the discipline has developed. But in 1996, did you have this opportunity to apply these more sophisticated or different stains to the material?

A. Yes.

Q. In fact, you did apply different stains to the material?

A. I did.

Q. Maybe you can help explain this, this is 236-007-021. What is that? Firstly, does that relate to Claire?

A. No, this is a picture from a textbook.

Q. What is that trying to indicate there?

A. This is the hippocampus, which is the structure that

we have been discussing because it's very important in memory, but it's also a part of the brain that is affected in cases of epilepsy. And this is the area of the brain specifically where, if you've had seizures, you can get damage here, which causes regeneration of cells, which seem to set up circuits which set up more seizures, so it's a very, very important area for us to look at in patients who have epilepsy.

Q. And I'm going to then ask you to look at the next page, which is 022.

A. Would you like me just to point out on that picture?

Q. Yes, sorry.

A. If we go back, we have talked about the dentate fascia, which I said may have been a little bit dispersed --

Q. Ragged?

A. A little bit ragged, yes. So in the middle of this picture we can see a very dark blue line, a sort of inverted U shape, which has the letters "DG" on it. That's called the dentate fascia or the dentate gyrus. That is that band of cells: that blue line is in fact composed of seven to ten layers of cells closely packed and they're stained with this blue stain, which stains up the nucleus of the cells rather nicely. So that DG layer is the most important one in terms of Claire's brain pathology and also beneath it there is a little H.

That's called the hilum, which is the end of a row of cells which go all the way out through CA4, 3, 2, 1, there's a big spiral of cells which curve in. So this is a part of the cerebral cortex, which during development, just rolls up a little bit like a Swiss roll and forms the hippocampus that we see in front of us. And all of these cells, the whole layer, are cells which are specifically vulnerable to epilepsy and also specifically vulnerable to reduction of oxygen supply to the brain.

Q. And then can I bring you to 022. Does this show Claire Roberts?

A. The two upper pictures, which have an "R" in the left hand corner, are from Claire's hippocampus. They've been stained with the GFAP stain, which demonstrates the astrocytes, which are the cells responsible for scarring in the brain. The two lower pictures were taken from a 10 year-old male who died very suddenly with no history of epilepsy, which presents a very similar aged control for Claire, where we would expect to see the normal baseline appearance.

Q. And what indicates the slight degree of scarring that you identified in Claire's slides?

A. If we look at the two bottom pictures first, you can see there's a black arrow pointing to the dentate fascia,

and in the bottom-left picture, there is an arrow pointing towards the left. There's a row of cells that are very pale grey-blue colour, and on the right side they're enclosing an area called the hilum, and that's seen at a higher magnification on the right.

Q. So the right is the same as the left, but just a higher magnification?

A. Yes, indeed. The same appearances are seen in Claire's brain at the top and stained with the same stain, but it was my impression that looking at Claire's brain, there are more brown cells in the left hand picture, in the area called the hilum, and they're extending processes through that dentate layer. There are more little fine processes going out through that C-shaped structure. And on the right side, we can actually see cell bodies -- they're called astrocytes because they look like stars -- and if you take the black arrow and just continue it down and go a little bit to the right, there are a couple of cells which have --

Q. You mean those things with the very dark centres with things radiating out? There are two that you can see to the right of the arrow; is that what you seen?

A. Yes, there's a dark centre and there is a tiny little blue spot right next to the centre, which is the nucleus of the cell, and what's radiating out are the astrocyte

processes. That's why they look like stars. There's certainly a little cluster here which are also extending down into the dentate fascia. So it's very subtle, but my impression is that there is more in Claire's hippocampus than there is in the control, and it's this subtle change which led me to the conclusion that there was very subtle hippocampal pathology, which would be consistent with her previous history, and it may been the basis for her vulnerability to seizures.

Q. So although you wouldn't have been able to find any evidence of the status epilepticus, you might have found some evidence of why she might have been vulnerable to it?

A. Indeed. And I want to emphasise that this is subtle on the GFAP stain and it was very difficult to see on the ordinary routine H&E. So it would have been perfectly possible to look at the H&E and say, "I can't see anything abnormal here". It's only by doing the special stains that the change was apparent.

THE CHAIRMAN: How confident are you that that's what it does show? I get the impression, when you refer to it as "very subtle evidence" ... Is there a difference between "very subtle" and "strong"?

A. Yes, there's not a great deal of scarring, but I think there is a little and I think that one of the

difficulties here is that we very rarely look at the hippocampus in patients who had a short history of epilepsy. The most common experience that we have as pathologists is to look at the hippocampus in patients who have a long history of epilepsy, who have uncontrollable seizures and have surgery to remove this after many years of seizures when there is severe pathology. But certainly this compares with what is described in the textbooks as the earliest, lowest grade of hippocampal sclerosis or scarring.

MS ANYADIKE-DANES: It's maybe your use of the term "subtle". Just so that we're clear on it, are you intending to convey how confident you are that it was there or are you intending to convey how much of it was there and the extent to which it's in its early stages?

A. I'm expressing the opinion that this is abnormal, there is scarring, but it's a very minor degree.

Q. So it's not that you're unsure of what you are seeing, what you're seeing is a process in its very early stages?

A. Yes, indeed.

Q. Thank you.

THE CHAIRMAN: So when you then go on to consider your ultimate diagnosis, you have to take into account the fact that the scarring which you've identified on the

further staining is to a very minor degree?
A. Yes.
MS ANYADIKE-DANES: And then if you were having a clinicopathological correlation, would there be some discussion between the clinicians and maybe even some specialists and the pathologists as to the likelihood of that level of scarring, which is what you have seen, translating into the kind of presentation that Claire had when she was admitted and throughout 22 October?
A. There may be discussion, but many forms of epilepsy don't have any real pathological manifestations.
A patient can have severe epilepsy without necessarily seeing any changes in the brain to cause them, and in fact I think the changes that I've described here are secondary, reactive changes, rather than the primary ones.
Q. The point that I really meant was: if you were in the position of Dr Mirakhur and Dr Herron, you've been set a task, "Look in the brain, tell us what you see, these are the particular problems that we thought that she had during her life", so you go off and you look. From their point of view, once they get your information are they not trying to see: now, that, whatever is the level of subtlety that's been described -- you've described this as in its very early stages -- Dr Herron and

Dr Mirakhur, for example, will have described the neuronal migration disorder as subtle, in its very early stages. Somebody has to try and put that together and express a view as to whether that means it is likely that her presentation resulted from some of that or something else.
So where is that process, what's the forum, if there is one, for the application of the evidence you have together with what was seen and observed of Claire so that you can end up with some sort of explanation for what happened to her?
A. The report and the information goes back to the clinicians and then they're in a position to integrate that with their observations and to say that that would explain her previous history, it would explain why she may have been vulnerable to seizures.
Q. And to the extent that this is all very specialist stuff and her clinicians may not be able exactly to reach a view as to whether the kind of slight scarring that you've noted there could have had any relevance at all for what happened to her that brought her in and caused all her difficulty over the 22nd, might it be that you bring in other experts to try and help with that or is this enough for the clinicians to be able to see the link themselves?

A. In my view, the pathology is, on this aspect, fairly secure and would explain a cause for seizures. I would expect the clinicians then to either come back and ask for further information, particularly a specific paediatric neurologist -- and I think a paediatric neurologist was involved -- to say this does fit with the kind of seizure history she had or it doesn't fit with the kind of seizure history she had. So it's really back to the clinical integration of the pathology into the clinical picture at whatever level the clinicians wish to pitch it.
Q. Thank you. If we go to the inappropriate ADH, that's also on your list of clinical problems. What is it that you think from the pathology you can bring to that problem?
A. I don't think we can bring anything at all to that problem. We can describe cerebral swelling, we can't say what the cause of that was unless there's something obvious in the brain itself, a tumour or something within the brain that is likely to generate swelling. Otherwise, whether it's due to inappropriate ADH or low serum sodium, we can't help with that. We really are looking at a fairly crude measure of brain swelling.
Q. So what in fact Doctors Mirakhur and Herron did with that is they referred in the "comment" part of their

report -- I can pull it up for you, 090-003-005. You see it there. They're talking about what's there that is suggestive of viral aetiology, and they go on to say:
"... with a clinical history of diarrhoea and vomiting, this is a possibility --"
This is the point I wanted to bring you to:
"... though a metabolic cause cannot be entirely excluded."
Is that the pathologist trying to signal this might in some way be related to your problem of SIADH or inappropriate ADH, but we can't assist further, we're just putting it there for you to try and see the extent to which that is something that you yourselves should explore further?
A. Yes, indeed. They're saying there's brain swelling, essentially, it could be infectious or it could be because of a metabolic disruption.
Q. So they've highlighted that, but that's not something that they can't advance themselves?
A. Indeed.
Q. They've been asked about it, so I'll ask you. Would it --
THE CHAIRMAN: Sorry. Are there cases where a metabolic cause can be entirely excluded?

A. Not by pathology alone, I don't think.
THE CHAIRMAN: Right. So that phrase "though a metabolic cause cannot be entirely excluded", could that be inserted into every comment?
A. I'm sorry?
THE CHAIRMAN: Could that be inserted into nearly all brain-only autopsy reports?
A. It could be, wherever you have brain swelling. We simply can't say --
THE CHAIRMAN: This may be just the nature of the beast, but I'm wondering, is it something which actually can give anybody a steer when they read the report?
A. I think the sort of steer it's giving is that if there is a problem with serum sodium and abnormal ADH secretion, that this may have been a cause of the brain swelling, but we can't tell from the pathology.
THE CHAIRMAN: Okay, thank you.
MS ANYADIKE-DANES: If that's what they wanted to point to, although you couldn't tell that from the pathology, is it something that should have been flagged a little more clearly, because essentially what they're doing is they're pointing to a completely separate mechanism for the development of her fatal cerebral oedema and not one that you would be in a position to find evidence of. And if that's what they're doing, would it not have been

better to have spelt that out a little more clearly and perhaps even refer to hyponatraemia?
A. I think that would be a very nice way to write a conclusion because it's taking all of the problems and examining them, each in order, and making a pathological explanation for each in order, which is really the whole point of the autopsy in any case. But it's something that isn't always done in that degree of detail.
Q. I think Dr Herron in his evidence, on 29 November, thought there might be some metabolic causes that you could exclude. We might find it at page 162. So this is me asking him essentially the same sort of question the chairman was asking you. Perhaps if we can bring up 161.

It starts really at 19. He says:

"They're obviously much more used to children who come in with metabolic diseases. There are consultant metabolic physicians ... I'm not sure if there were then. They would be aware of the different spectrum of diseases that could cause a presentation like this in a child like Claire much better than I could."

Then he goes on to say:

"I think the main one would be Reye's syndrome, but none of us found any evidence of that in the brain ... There are thousands of metabolic diseases."

And he says that you couldn't be spending your time looking and checking all of them just for the purposes of saying that you have excluded them. And then I ask him at line 12 on page 162:

"Do you seek to exclude the ones that can be excluded to help refine things for the clinician?"

His answer is that he really thinks that Reye's syndrome is the one and it's very rare and he has only really seen two cases in his lifetime's experience.

Does that mean that there are some things that come under the heading or the category of metabolic disorder that you could exclude and the ones that you thought, even on the rare spectrum, are the most likely to present themselves or the easiest to exclude, and you simply try and do that?
A. Yes, indeed, one could look for certain disorders. I think in the specific case, in Claire's case, that conclusion probably was related to the ADH question, but it wasn't spelt out.
Q. That's I suppose the point I'm really asking you. If you thought that you had some particular concern to look for a metabolic disorder, particularly if it was a named one, would you not identify that clearly so that people would know that that was excluded?
A. I think one would as far as it is possible, and there

are certain metabolic diseases that do leave their footprints in the brain and one can identify the pathology. I think that in this case, in Claire's case, it would have been helpful to be more specific, saying that the specific metabolic question that was asked, the cause of the cerebral swelling, cannot be diagnosed pathologically, and therefore we cannot say whether or not that was the cause of the brain swelling.
Q. And then if we pause there because there has been a reference in Claire's medical notes and records to hyponatraemia. The issue, as the clinicians in their evidence have discussed it, is really whether you think that was a product of something else happening, let's say the SIADH, and that's certainly what Dr Webb thought, that the SIADH led to the hyponatraemia and that developed and so forth and the end result of that was cerebral oedema and coning. Or you might think that the hyponatraemia itself led, as an independent line, to the cerebral oedema and therefore was the cause rather than an effect. The information that the pathologists have got is really only to lead them on one line of that, which is that it was effectively a product because they're told about the inappropriate ADH.

If you are starting to think about other things that you can't necessarily see the evidence of and pathology

that could be independent causes of the cerebral oedema, given that cerebral oedema is obviously the final cause of death and it's listed as the top clinical problem, to what extent do you get into any more detailed speculation about the way in which hyponatraemia might lead to cerebral oedema?

A. I think it's something that we try and steer clear of, and I think that's probably why that remark was made as pushing off the metabolic conditions because we wouldn't be able to add anything to the argument as to what sort of disruption of sodium, whether it was primary or secondary, was underlying the cerebral oedema. That's something we just couldn't start to discuss.

Q. Because whichever way it went, it is not something you could distinguish on the pathology?

A. Exactly. We have a swollen brain. And Dr Herron has mentioned Reye's syndrome and I think there was a comment about the mammillary bodies in the brain not having proliferated capillaries, which shows that they were looking for some sorts of metabolic conditions, but they didn't set it out in their commentary that they had looked and not found evidence.

Q. Yes.

THE CHAIRMAN: So the degree to which the comment could have been more helpful is actually very limited?

A. I think they could have said, "We've looked for Reye's syndrome, we see no evidence, and we cannot differentiate the different causes of metabolic --

THE CHAIRMAN: It doesn't seem that any more specific comment would have really taken the report much further?

A. I don't think so. I think they were trying to avoid getting into that area.

THE CHAIRMAN: Yes.

MS ANYADIKE-DANES: Thank you.

If we can deal with the encephalitis now because that's the fourth thing that's queried. Of the four clinical problems, that has a query over it. If you'd received the autopsy request form in that way, what would that have indicated to you? Let me pull it up, 090-054-183 and 184. You can see that that's queried both at the clinical diagnosis, "query underlying encephalitis", and, as a problem, it's queried in the fourth rung, "query viral encephalitis". Is that of any significance if you were to receive a form like that?

A. Clearly, it was very significant to Dr Herron because he did the post-mortem in a safe environment, so he was very concerned that there was an encephalitis and he was --

Q. I meant it in a different way. I meant the fact that that is the way the information is coming to you from

the clinicians so that is how they have chosen to frame it. Is that significant that it's queried in that way or not?

A. It suggests that they're not at all sure of the diagnosis. Is that what you mean?

Q. That's what I was asking. I'm asking how it would suggest itself to you.

A. It suggests here that we have a problem of cerebral oedema, we have status epilepticus, which seems to be the more important clinical consideration, and is this perhaps secondary to an encephalitis, which seems to be their least favoured diagnosis.

THE CHAIRMAN: If you're the receiving pathologist, does that give you an uncertain steer about something you should be alert to?

A. Oh, you should certainly be alert to it.

THE CHAIRMAN: Okay.

MS ANYADIKE-DANES: Then how do you go about seeing whether you have got the evidence of that when you are examining the slides from the blocks made?

A. One is going to look to see if there is evidence of inflammation in the brain.

MS ANYADIKE-DANES: Mr Chairman, I was then going to ask Dr Squier to look at some of those slides and explain them. That may take a few minutes. I am conscious of

the time. I'm in your hands.

THE CHAIRMAN: I think we'll go on to 1 o'clock, we'll take a 45-minute lunch, and we'll continue with Dr Squier until about 2.50 and then break for the link to be set up for Professor Harding in Philadelphia.

MS ANYADIKE-DANES: Thank you very much.

You first are looking at the H&E slides because that's the basic stain that's applied.

A. Yes.

Q. What do you anticipate that, if you have a viral encephalitis, your H&E slides will disclose?

A. They will show cells which have come from the bloodstream across the blood vessels into the brain tissue to react to the presence of an infection.

Q. Cross the blood-brain barrier?

A. Yes, indeed. So there could be infection in the meninges, which are the membranes surrounding the brain, or there can be infection in the brain tissue itself. One is meningitis, one is encephalitis, and commonly one sees meningoencephalitis, a combination of the two.

Q. And when you looked at the slides that Professor Harding saw, which were the ones prepared by the pathologists in Claire's case, did you see evidence of that?

A. No, I didn't.

Q. Did you prepare your own slides, applying different

stains to see if you could see it?
A. Yes, I did.
Q. And what stains did you apply?
A. I did the H&E stain, I did a macrophage marker, CD68.
Q. What is that supposed to show you?
A. It will show two sorts of cells. One, there's a resident population of cells in the brain there for immune surveillance, they're there looking for foreign proteins. Those cells are called microglial cells. If they're stimulated, they look a bit bigger, a bit different, and they then transform into macrophages, which come along and respond to foreign material. And then more cells will come from the bloodstream into the brain across the blood-brain barrier. Those will be both macrophages and lymphocytes, which are responding to some sort of tissue damage or some foreign protein --
Q. So that kind of response that you see, you would be looking for that to see if there has been some sort of foreign agent in there to which the cells are now responding to. So you're looking for the response as well as the agent itself?
A. Yes, one can look for the agent, one can look for the response, but one must also bear in mind that when tissue is damaged and cells break down, proteins are released from those cells, which are not normally

present in the environment and that will also stimulate a macrophage response.
Q. These different stains you apply, are they targeting any of that sort of response?
A. Yes, indeed, the CD68, which is one of the stains I used, specifically looks for the microglial macrophage response. I don't think I did any lymphocyte markers myself. I think that's the only inflammatory marker that I used in my stains. The reason being that there wasn't any really good evidence to do any further stains. I'm sorry, I don't have my report with me.
Q. I'm just going to help you by bringing up some of the slides. You received, I think, all in all, 10 images from the pathologist. If we pull up 236-007-032. Can we just increase that a little bit?
This is part of the nine photographs from the stains themselves that you received. You've also produced a little comparison series of slides between those slides thought to indicate encephalitis and other slides showing encephalitis. We'll come to those in a minute. This is what Dr Herron and certainly Dr Mirakhur were looking at. Can you explain the extent to which that indicates any inflammatory response?
A. First of all, to explain where we are: in the centre is a big while hole, that is a blood vessel. It has no

blood in it so, so it's an empty white space, and it's bounded by a thin, pink line, which is the endothelium, the lining of that blood vessel, which is best seen down at the bottom right where it's a sort of wiggly line and there's a space on the tissue side of it as well, which is something we see from time to time, just a little space around the blood vessel.
The tissue itself -- the majority of this picture is pink brain tissue with spotted, round blue cell nuclei. That's the brain tissue itself. But you will see that around the blood vessel wall, there's a scattering of smaller, darker, very round nuclei. They're just a little more round and a little smaller and darker than the cells of the brain tissue. Those are probably lymphocytes. They've probably come across the wall of the blood vessel into the space around it. And it's important to recognise that we all have some cells there all of the time constantly patrolling, looking for foreign proteins. So it's normal to have a few cells in that space around blood vessels. In this case, they are certainly more numerous than usual, but they are certainly not anything that would raise alarm in my mind, particularly if we have a brain that's swollen and may have been subject to reduced oxygen supply while the little girl was on a ventilator. That's something which

could be secondary simply to the sort of problems that the brain would be experiencing during ventilation.
So that's one thing. They could be the normal patrolling cells, which are a little bit enhanced. The two other things that we look at are: are they specifically directed at the blood vessel wall, is this a vasculitis, a condition where the blood vessel wall is damaged? And the answer is no, because the blood vessel wall, as far as we can see it, looks intact. There's no inflammation or necrosis in that blood vessel wall. The other more important point is, if these cells are coming in from the blood in to the brain because the brain has a virus in it, they will be going into the tissue of the brain and seeking out and destroying those cells which have virus in them. So we would see those cells extending into the brain tissue itself and they're not; they're simply confined to that space around the blood vessel wall.
Q. You mean, you expect to see them moving out, radiating out towards the rest of the brain, if I can put it that way?
A. Yes. We would see changes in the brain tissue. First of all, we would see cells that look as if they're dying, we would see --
THE CHAIRMAN: Could you slow down a little bit?

A. I'm sorry, yes. We would see reactive blood vessels, maybe congested, widened, dilated blood vessels that are irritated by this, and we would see collections of these cells in the brain tissue, destroying cells that contain viruses.

MS ANYADIKE-DANES: There's actually an enhanced part of this slide, which I think one can see at 236-007-033. I think that's a part of that; am I right about that? Is that white thing still part of the blood vessel?

A. I think it's another blood vessel, and in fact here what we have, I think, is a big white band down the middle of the picture, which I think is the space around the blood vessel. That can just be fluid because we have got brain swelling.

Q. So you have a close-up, if I can put it that way, for the layperson, and you can see more of those blue dot things. Maybe you didn't see it so clearly in relation to the other blood vessel, but in this blood vessel does that help to indicate this is an inflammatory response?

A. What this shows is, first of all, you have a slightly bigger blood vessel so the streak down the middle, slightly bowed towards the left, is a thicker blood vessel wall. Again, the blood vessel wall is perfectly intact, there's no evidence that the blood vessel wall is being damaged, so it's not a vasculitis. We can also

see very clearly, particularly on the left half of this picture, that the brain tissue there is not infiltrated by these cells; they're just around the wall of this blood vessel. So they may be a little bit enhanced, but they're the sorts of cells that we have normally, but there are perhaps more than we would except to see.

And there are two points: one, there is no infiltration of the brain tissue so we don't have any evidence of an encephalitis; also, the pictures sent by Dr Mirakhur and Dr Herron, these pictures are in the brain itself, they're not in the meninges, and I didn't see more than perhaps two vessels, in all the sections I looked at, which had this sort of appearance, and I certainly didn't see any increase in cells in the meninges. So there was no meningeal aspect to this. All we're seeing is a few extra cells around a couple of blood vessels in the brain.

Q. In fairness to Dr Herron and Dr Mirakhur, there are other slides. If we can just go quickly through them and you can tell us whether that changes the picture at all or not. 034.

THE CHAIRMAN: Sorry, I think you said it didn't change. You have given a description of the pictures, is that right, and that you did not see more than perhaps two vessels, in all the sections you looked at, which had

this sort of appearance and you didn't see any increase in cells in the meninges; is that right?

A. Yes, that's true.

MS ANYADIKE-DANES: Yes, Mr Chairman, but Dr Herron and Dr Mirakhur have thought that they have seen, so in fairness to them I was just going to -- I think there are three more of these for you to see whether this, in your view, lends any support at all. Do you know what that is or where we are with that?

A. It's a bit of pink brain tissue.

Q. No evidence of any inflammation there at all?

A. No.

Q. And then 035. What about that?

A. This is also brain tissue. We can see on the top of the left a little sort of curvy bit of dark blue. That's called ependyma. That's lining the fluid cavities inside the brain. No inflammation. Nothing in there, apart from a swollen brain.

Q. And then just quickly 036.

A. A bit of swollen brain.

Q. 037.

A. A little bit of brain here. At the bottom left-hand corner, we can see some nice big nerve cells. They look perfectly happy. There's no inflammation in or around them. In the middle of the picture, running

horizontally, is a little tiny blood vessel with a lot of space around it. This is typical of brain swelling, as are all the other little white spots. Those are swollen brain cells. There is no inflammation around that blood vessel. No inflammation anywhere, it is just a little bit of swollen brain.

Q. One more. 038.

A. This is brain tissue on the right, which is pink. Then there's a band running from the middle of the top down towards the bottom right-hand corner, which is clear. That's a space. I think that's where the meninges, which are the membranes surrounding the brain, have separated from the brain surface, and the majority of this picture is of the meninges, the arachnoid tissue, which is the covering of the brain. There's a scattering of cells in there. They may be a little bit more numerous than one would expect, but they're diffusely found, they're not clustering around blood vessels, they're not showing the appearance of meningitis.

When I looked at the brain myself I thought this was coming from around the pituitary region, and I think this is just the normal appearance of the membranes in that area. I certainly wouldn't have called this an inflammatory meningitis.

Q. 039, the final one.
A. A bit of brain.
Q. Presumably there is a scale of inflammatory response from not very inflamed to really quite acute. And if I can bring up 236-007-016. On the left hand side is the first one that you were explaining to the chairman about, and on the right-hand side, this is encephalitis, is it?
A. It is.
Q. And is that a blood vessel also? What is that bit in the centre, the collection of dark cells.?
A. It's a section of brain and the round bit in the middle is a blood vessel, surrounded by a huge collection of inflammatory cells. These are cells coming into the tissue in response to some sort of damage in the brain tissue itself. It's a severe example, but I wanted to make sure that we could see both ends of the spectrum.
Q. You said you applied your own stains and, even then, you couldn't see anything.
A. That's correct.
Q. So you cannot see any evidence for what is described in the autopsy report -- sorry, to get the exact wording of it -- which is the "low-grade sub-acute meningoencephalitis".
A. That's right. There was certainly nothing in the

meninges that would have caused me to think twice about an infection and there were a couple of vessels, such as the one on the top left, in the brain tissue, which caused me to stop and think. I thought that, on balance, because there's no involvement of the brain tissue itself -- and I think I did provide a picture which shows what we would expect to see because we only saw these cells restricted to the space around the blood vessels -- that I would not have made any diagnosis of encephalitis because this degree of increase of inflammatory cells could be a response to the brain swelling and hypoxia and ventilation.
Q. Thank you. Dr Herron, to some extent in his evidence, was rather diffident about whether there was -- it's possible he said that there actually wasn't any evidence of it, it was such a low level. And in fact, when he was asked to measure it on a scale of 1 to 10, he had it as 1 or 2. And when Dr Mirakhur was asked the same question, she accepted what he said, but she said she would have had it closer to the 2 end, if I can put it that way. I think Dr Mirakhur was asked:
"If you were being asked what level would it have to be at in order to be thinking of it as having been a cause of or contributing to her death, the cerebral oedema from which she ultimately died."

Dr Mirakhur's evidence was she thought it would have to be at about 5. So neither of them thought that what they were seeing there was something that had contributed to Claire's death.
THE CHAIRMAN: Do you agree with them on that?
A. I do, but I do want to add a caveat, and that is I think it's perfectly possible for a child -- and the younger the child perhaps the more likely -- to have an overwhelming infection, a sepsis, where the infection has got into the blood, which can cause a child to die very suddenly and we won't see any evidence of it in the brain, or there will be just very few cells in the meninges. So I don't think that we could exclude the possibility of an inflammatory condition, even involving the brain, which has caused very rapid death.
MS ANYADIKE-DANES: All you could say is you can't see the evidence of it in the brain?
A. Exactly, yes.
THE CHAIRMAN: What's the difference then between you and Dr Herron and Dr Mirakhur? Their evidence is that they found very little evidence of this. You say you don't see any, but you all agree that it does not suggest that encephalitis was the cause of death.
A. I think we all agree that the evidence that we have here would not support encephalitis as the cause of death.

THE CHAIRMAN: Right.
A. I would add the caveat that it may cause death without showing any signs at all.
THE CHAIRMAN: Yes. So they have interpreted the slides that you have been looking at to show something more than you have done, but the end result is agreement between you, subject to your caveat?
A. I think we do all agree now, yes. But I would certainly not make a diagnosis of encephalitis because there was no evidence of this inflammation extending into the tissue of the brain, it was all just around the blood vessels.
MS ANYADIKE-DANES: Have you seen a report from Professor Cartwright?
A. Yes, I think I have.
Q. Professor Cartwright was a little concerned about the cerebrospinal fluid result and thought that that might be indicating something, and I think in fairness to him he was rather surprised that nothing, so far as you and Professor Harding were concerned, had shown at autopsy, and probably a little surprised that it was as low grade as Doctors Herron and Mirakhur have described it.
Is the interpretation of the results of CSF something that you involve yourself in or would you bring an expert in?

A. I would bring an expert in. I don't look at CSF at all.
MS ANYADIKE-DANES: Thank you. My next step would be to ask you about the neuronal migration disorder. It may be that we can --
THE CHAIRMAN: We'll pick that up at 1.45.
(1.00 pm)
(The Short Adjournment)
(1.45 pm)
(Delay in proceedings)
(1.55 pm)
MS ANYADIKE-DANES: I wonder if we could go back to something that you said towards the end when you said that there could be some sort of catastrophic failure that happened so quickly and was so overwhelming that you did not see any evidence of it or the footprint of it on the pathology. Is that just one of those things, because it's a residual category, it's always possible for something like that to happen, or would you expect to see evidence of it anywhere else?
A. I think that one may not see any evidence of it as a pathologist. There may be biochemical or serum markers, raised levels of white blood cells and so on in the blood, which may give you the evidence, and by looking for organisms. Certainly, in the post-mortem series at Great Ormond Street Hospital, they have shown

that a number of babies who have died in otherwise unexplained ways may have certain organisms in the body which are known to be pathogenic, but there is no histological evidence of a response to those organisms; they seem to have come in and done their damage so quickly that the child has succumbed before the pathological response is manifest.
Q. So if you haven't got the evidence on the pathology, if I can put it that way, then in order for that to be a hypothesis which you can't test on the pathology, but you would be expecting, if it was going to be continued on, for there to be at least some basis for it somewhere else?
A. One wouldn't be able to propose it as a valid or reliable hypothesis unless there were something else such as blood cultures or white cell counts, clinical history, the temperature and so on, which would give you picture which was consistent with that.
Q. And I suppose in Claire's case what you might say is, on what had been measured and received so far, one didn't see any evidence of that necessarily, and if there may have been other things that could have shown that, those things don't appear to have been tested or done?
A. As far as I'm aware, but I'm not sure how much of the clinical testing would have supported that hypothesis.

It was clearly raised as a clinical diagnosis and there must have been some clinical evidence on which that speculation was based.
Q. So is that a little bit like Doctor Mirakhur's and Herron's flag, "Well, there might be, of course, some metabolic disorder", then you say, "There might be an overwhelming response that we haven't been able to detect on the pathology"; is it a bit like that?
A. Yes, it's too quick. It's happened so fast the body has succumbed and the individual tissues have not yet undergone their process of reaction, so one would want to look at those other features like the clinical presentation and the white cell count.
Q. It may not be you who would do it, it might be a microbiologist, it might be any specialist in another discipline, but if you were wanting to see that, by the time the pathologists have completed their work, is it too late to get the evidence for that sort of thing and are you therefore confined to the tests that were done while she was still alive and the lumbar puncture?
A. Yes. I think one has to go back to those tests then.
Q. If you had wanted to maintain that kind of hypothesis or at least test that hypothesis, were there further tests that could have been carried out if it had been thought about -- not necessarily by you -- at the

outset?
A. During life when Claire was a patient?
Q. That's one, during life.
A. Yes, I think first of all, during life, the tests one would do then would be blood cultures, doing a lumbar puncture to look at the CSF, looking at the blood counts -- and at post-mortem, looking at CSF, for example.
Q. And at post-mortem looking at CSF. In fact, they did look at the CSF at post-mortem and her white cell count had fallen during life, during admission. That might not be an issue that you can advance for us, but I wonder if you can comment on something that Professor Cartwright, who was engaged by the inquiry as its expert microbiologist, wanted to put to Professor Harding in particular. He had asked for a question about the fulminant encephalitis to be put to Professor Harding. And during his evidence, he asked for a further question to be put to him and I am going to put the same to you to see if you can assist with it. It's the transcript for 7 November 2012 and it starts at page 84.
You can see starting at line 4:
"What I would hypothesise here or the hypothesis that I would put to Professor Harding would be: can you

get a massive rise in intracranial pressure consequent upon cerebral oedema before you have had a chance for white blood cells to migrate into the brain matter?"

Then he picks it up again at line 13:

"What I'm interested in is: can you exclude the possibility that you could have a failure of white blood cells to infiltrate the brain matter after a period of three days?"

Are you able to assist with the queries that Professor Cartwright is raising there?

A. Yes, I think essentially, probably, he's asking the question that I think I've been putting forward, that you can have not necessarily just brain swelling, but the body can react to the presence of an overwhelming infection in such a way that death occurs before the cells have got into the brain tissue. And secondly, he adds in this period of three days:

"What I am interested in is: can you exclude the possibility that you would have a failure of white blood cells to infiltrate the brain matter after a period of three days."

I think the important point here is to remember that Claire was being ventilated at that time. And once you put a child on a ventilator -- or any patient who has brain swelling -- you're actually breathing for the

patient. The brain can therefore become very, very swollen inside the head, so swollen that the pressure in the head will actually prevent any fresh blood coming to the brain because the pressure is such that it's exceeded the blood pressure.

If that's the case, then fresh blood can't come to the brain so it can't bring those inflammatory cells into the tissues. So all of the inflammatory and reactive changes we see in the brain will be muted in a patient who is nursed on a ventilator with an extremely swollen brain.

Q. His reference to three days is actually, I think, what Professor Cartwright was envisaging is that she had come in with something that started as some sort of viral infection and that would have been on the 21st, and she has died by the 23rd, and I think the autopsy -- at least the brain is removed on the 24th. And really what he's asking himself is: is it possible to have had an identification of a viral encephalitis or some sort of viral infection? It had apparently produced the kinds of effects and contributed to her death in the way that the clinicians thought it was, and yet you see no evidence of it despite three days, if you like, and he was thinking that that would be a sufficient period where you might see some sort of evidence of it in the

brain. I think that's why he's stressing the three day point.

A. Yes. I think there are two points to consider here. One is, as I've just said, if the brain swells rapidly so the blood can't get into the brain, then we won't see the same inflammatory response. The other point is, and I think this is something that Professor Harding already touched upon, that for an encephalitis to have produced so much brain swelling, it would have been quite outside his expectation that one could have had that much brain swelling due to an encephalitis without any other manifestation, the sorts of things I've been discussing this morning of cells infiltrating the parenchyma. And I think we have to take one step aside at this point and look at the possibility that a separate cause of the brain swelling was also operating.

If Claire had had some kind of infection that was going to run its course as a fairly mild infection, but on top of that her brain was caused to swell for a completely separate cause, then the brain swelling might not be an indication of the severity of that degree of encephalitis, but it may have been supervened on a modest inflammatory condition that may have triggered the onset of her illness and admission or triggered seizures.

Q. I see. So the encephalitis may not have been of the severity to have caused the extent of her cerebral oedema, but it's there. The actual development of her cerebral oedema and why it reached the fatal stage is something entirely separate?

A. I think it may be. I would also express caution over saying that the encephalitis is there because I don't think it is there.

Q. I understand. I see what you mean, yes. The infection is somewhere, it just hasn't reached the brain?

A. That is one hypothesis. That's one suggestion because we know there are cases of children and adults who die very suddenly of overwhelming infection and it may have involved the brain or caused brain swelling, but we don't see any evidence.

Q. If the infection is somewhere, if a full autopsy had been done, is it something that you would expect to be found somewhere?

A. It's possible.

Q. If we just pull up, so that we see that you've been commenting on this part of Professor Harding's report, 235-002-001. Is what you've been explaining in this part of his answer:

"Given the marked degree of brain swelling noted clinically and confirmed at post-mortem, I consider it

extremely unlikely that microscopic evidence of encephalitis would not be evident by three days. I have seen it occurring in 36 hours"?

That's ever supposing that that brain swelling is the result of the encephalitis. That's your point.

A. Yes, because the question actually, just above that, is:

"Whether in your experience an encephalitis causing cerebral oedema, coning and death."

Q. Yes.

A. I think we have to just be careful that we might have to separate those two.

Q. I understand. Then I wanted to take you to the evidence that Doctors Mirakhur and Herron had found in relation to neuronal migration disorder. If we go to their slides, I think the particular slide is to be found at 236-007-040.

Just before you tell us what you see in that slide and how you interpret it, can you very briefly say what neuronal migration disorder or defect is and what the significance is in finding things migrating or not migrating, as the case may be?

A. The central nervous system, the brain, starts off a little bit like a tube with a hole in the middle and the lining of that tube is very similar to the lining we see on the left side of this picture. There's a white

space and then that nice, neat row of dark blue cells. That's called the ependyma. In the developing brain, beneath that layer, is a mass of germinal tissue. This is tissue where all the cells that will form the brain divide. They then move from that position to the cerebral cortex.

So for every one of us, in all of our brains between six weeks after conception to about 20 weeks after conception, cells are migrating from around the ventricles to their place in the adult brain. It happens to all of us and it's an essential part of brain development.

If something impairs that migration and the cells can't go to the cortex, they may be caught up somewhere along that pathway and some of them may stay where they started just underneath the ependyma and never start that journey. The significance is that it unbalances the numbers of cells we have in the cortex of the brain and may predispose to learning disorders, to epilepsy, to neurological manifestations. I think those are the two predominant ones: cerebral palsy and epilepsy.

So neuronal migration disorders have, in the last couple of decades, been recognised as a very important kind of malformation, leading to serious disorders in young children and adults.

Q. Is it possible in patients or persons who have perfectly normal presentations nonetheless to have cells that haven't migrated all the way across?

A. All of us have a few cells just there in that position beneath the ependyma. Little clusters of them which are residual, which we would have all ignored until a few years ago, because now they're being recognised as a very important potential source of stem cells. So there's an enormous amount of work going on in these areas, seeing whether these cells can be persuaded to start to mature and differentiate into cells that could go in and take over in conditions like Parkinson's disease or dementias, if we could persuade them to start all over again and migrate out and replace cells which are dying because of chronic disease. We've always known they're there and anyone who looks at baby brains will see little clusters of cells beneath the ependyma quite frequently.

Q. If we look at this slide here, which I think is one of the images or maybe the image from which Dr Mirakhur formed the view that it evidenced neuronal migration disorder and that allowed her to reach a conclusion that there might be some sort of evidence for Claire's developmental delay. Can you interpret this slide for us, so far as you understood it when you saw it?

A. On the left of the picture, we have a white space. That's the ventricle, the fluid-containing compartment within the cavity of the brain. Running top to bottom, is the ependymal cell layer -- that's a barrier between the fluid in the ventricle and the brain tissue -- and, on the right, we have brain tissue.

In that brain tissue, we can see one big cluster of cells just above the halfway horizontal line, as it were, right in the middle there, and a couple of smaller ones below that. Those are small undifferentiated cells, little dark blue cells that don't tell you that they're any particular kind of cells. They're rather undistinguished looking cells and they are in the position where all of the germinal cells would have been in the foetal brain. So they're residual from that and they're perfectly normal.

Q. If there were more of them there yet?

A. If there were more there, they would tend to be a mass, they would tend to push the lining of the ventricles, so it wouldn't be nice and straight, it would be pushed out by a cluster of cells there, and they usually tend to look a little bit more differentiated. You can see they look like nerve cells.

Q. I understand. And the implication of seeing more of them there is?

A. It suggests that there hasn't been complete migration. So if cells are still there and they haven't gone up to the cortex, what I would do is I would look at the cortex and say: does it look normal, does it look as if the cortex hasn't formed properly, has it got a nice, neat lower border, are the cells all beautifully lined up as they are in the normal cortex, or is there some subtle abnormality there which we should be looking for because that's where we're likely to have a site which might generate epileptic seizures?
Q. This was thought to be quite subtle as well. Why does this not come down to a matter of judgment? Dr Mirakhur looks at it, she thinks she sees the cells in a position that she wouldn't expect to see them for a child of Claire's age. You look at it and say I think that's all perfectly normal. Does that not all amount to a matter of judgment?
A. I think that this doesn't come anywhere near the basic criterion for diagnosing a neuronal migration disorder. I don't think it's a matter of judgment; I think this is normal appearance. It's perhaps a matter of not seeing enough brains or not looking -- looking for it. We only see the things we look for. So if she hasn't in the past regularly looked at this, then she may well just have been surprised by it.

Q. Is this something that you are looking at regularly?
A. Oh, all the time. Much of my work has been on looking at neuronal migration disorders. I started publishing on them in the 1980s because it's something that I see every day -- or I see normal migration every day and I look for malformations.
THE CHAIRMAN: Can we go back a few steps?
Mr and Mrs Roberts don't accept this, but Dr Steen has said one of the reasons why she suggested a brain-only autopsy was that something might be revealed on it, which would explain Claire's problems in her early life, which had given her some degree of limitation. As a starting point, that's perfectly fine, isn't it?
A. Yes.
THE CHAIRMAN: And to include that as a basis for the brain-only autopsy would be entirely legitimate?
A. Yes.
THE CHAIRMAN: So the only question is, if I understand it correctly, that Dr Mirakhur and Dr Herron interpreted this to give some indication of what had happened to Claire when she was an infant, and you disagree with them that that evidence is there.
A. I do, yes.
THE CHAIRMAN: Right. Does that otherwise affect the

autopsy report --
A. No.
THE CHAIRMAN: -- in terms of Claire's death?
A. No, this is not directly related to death. If we had a neuronal migration disorder, we could then work through the process of saying that means she had an abnormal brain, she was prone to have seizures, even a minor infection might have caused her to have seizures, and then that started the downward spiral. So it would support that path of diagnosis.
THE CHAIRMAN: But those points that you have just made, we do know anyway, don't we, because we do know she had a potential for seizures, which not all children do?
A. Yes, that's correct.
THE CHAIRMAN: So you don't need this element of the autopsy, to go looking for that; you know from her medical history, without this, that she had that weakness or liability --
A. Yes.
THE CHAIRMAN: -- which other children are lucky enough not to have?
A. Yes.
THE CHAIRMAN: Okay, thank you.
MS ANYADIKE-DANES: Thank you. I think in view of that, Professor Harding agrees with you. In view of that, it

may be that we can move on because you've explained very clearly in your report why you don't see it there. You've provided photographs of slides that would show you what it would look like if you had seen that there, and that's in your report. And in any event, I think certainly Dr Mirakhur has conceded that it isn't something that she thought necessarily explained, if I can put it that way, what happened to Claire during her last admission.
So then there are a few points that I would like to ask you out of the evidence that you gave about the slides. One is that the slides that you saw, that had been prepared by Doctors Herron and Mirakhur, they are a number of years old when you actually receive them. They made them towards the end of 1996 and you received them for your report in 2012. So they are of some antiquity for you. Do slides degrade over time in a way that they become less reliable as to what they're showing?
A. In general, the H&E is very reliable and that will last for many, many years. The immunocytochemistry may fade and it's always advisable to restain sections if they look as if they're not as bright and as crisp in giving you the expected results.
Q. Did you think the quality of those slides that you got

was such that you could look at them and express a view on them in terms of what Dr Herron and Mirakhur had said?

A. The H&E sections were perfectly fine. I did in fact cut and restain them, but the original ones had not deteriorated at all. I was concerned that some of the immunocytochemistry was not specific and had probably faded.

Q. What did you do about that?

A. I restained those sections which I thought were relevant.

Q. And if you restained them, does that now mean they're of a quality that you can assess and reliably take a view on?

A. I think so, yes.

Q. If you'd had a concern about it, would you have indicated that in your report?

A. Yes.

Q. You, I think, had expressed a view as to the hippocampus as really what you'd have been wanting to look at in terms of epileptic activity and so forth. Do you know exactly where all the tissue blocks that were provided to you came from?

A. No, I don't know where they all came from. Hippocampus, the mid-brain and various other structures are readily

identifiable, even on an H&E stain. It's quite clear. Like this picture, image 10 is clearly from the ventricular wall, but I have no idea from which part, and there were many blocks which were not labelled and I could only say these are cerebral cortex and white matter. I don't know where they're from.

Q. I wonder if I could put to you Professor Harding's report, the report that he prepared for the PSNI. You've clearly seen the more recent statements from Dr Herron and Dr Mirakhur, where they identify differences that they see between the views that you express and those of Professor Harding. In your most recent report, you are not clear that there are significant differences between you, but maybe you can help explain by responding to some of the conclusions that Professor Harding reaches.

So if we could pull up 096-027-359, and alongside it pull up 360. Up at the left-hand side, that's what Professor Harding is identifying he received. Of course, he received the autopsy report as well, and a letter from Dr Walby, giving him further history, and that's on the previous page, but we don't need that. That identifies the slides that he said he saw and you've also recorded having seen those in your witness statement -- I think it's your August witness statement.

If we now look at his examination. He says, as you do, that the sections aren't anatomically identified. Dr Herron said that's because he knew where they came from and he wasn't anticipating that anyone else was going to have to look at them.

He says:

"There is no evidence of meningitis or encephalitis."

And you would agree with that?

A. Absolutely, yes. I agree.

Q. He's referring to:

"... the numerous blocks taken from the cerebral hemispheres. In these sections, there is no evidence of meningitis or encephalitis."

Which he is defining as the inflammation of the brain and its coverings, and you'd agree with that?

A. Yes.

Q. Then he says:

"There is no evidence of haemorrhage or infarction, ie stroke."

You would agree with that?

A. Yes.

Q. And then dealing with the anatomy of the brain:

"There is no convincing evidence of malformation."

A. Yes. I agree.

Q. Then he goes on to say:

"Occasional neurones are present in the white matter. This is a normal finding."

Before you comment on that, is that his reference to what Dr Mirakhur has referred to as neuronal migration, or is that something else?

A. That's very difficult to say. Because she's so brief in her description, it's hard to say exactly what she's depending on.

Q. Okay. But then if you can't identify that as a reference to neuronal migration, how do you comment on "occasional neurones are present in the white matter"?

A. We see them all the time, just scattered nerve cells in the white matter. They're probably nerves that are responsible for controlling the blood vessels.

Q. And you would agree with therefore that that's a normal finding?

A. Yes.

Q. Then he says:

"The only substantive abnormality is the presence of scattered neurones showing hypoxic change."

Can you help us to what he's referring to there?

A. Yes. Certain cells throughout the brain, somewhere in the cerebral cortex -- I can't remember exactly where the rest were, but probably in the brainstem and the

cerebellum -- oh, the cerebellum wasn't sampled. Probably in the brainstem.

THE CHAIRMAN: Doctor, sorry, slow down.

A. I'm sorry:

"Scattered nerve cells throughout the brain showed a change in their staining pattern."

They were rather pink in colour and the nucleus was dissolving. These are the earliest changes of hypoxic damage.

MS ANYADIKE-DANES: You saw that?

A. I saw that.

Q. What did you relate that to?

A. Terminal changes: collapse, lack of blood supply to the brain, a period of ventilation.

Q. So any number of those things could produce those terminal changes; you're just seeing the fact that cells are dying essentially?

A. Yes, completely non-specific.

Q. Then he says:

"The basal ganglia and the thalamus as well as the hippocampus are similarly unremarkable."

Do you agree that the hippocampus is unremarkable?

A. I agree that, on the H&E stained sections, it would be unremarkable.

Q. And you were able to see distinction in them that made

them something worthy of comment because you applied further stains?

A. That's correct.

Q. Then he says that:

"Sections from the brainstem and the cervical spinal cord are unremarkable."

A. Yes. My only additional comment there was that there was a little bit of cerebellar tissue adjacent to the cervical spinal cord, the upper levels, which as I mentioned earlier, is an indication that there had been coning.

Q. There had been coning? Can I just ask you about that reference to the spinal cord because it came as some surprise to the family that there was any spinal cord at all. What's being referred to there as the spinal cord?

A. The brain is in continuity with the spinal cord. Up here at the back of the head (indicating), the part that we call the brainstem becomes the spinal cord and usually the top couple of centimetres of the spinal cord will be removed with the brain at the time of autopsy.

Q. So that doesn't mean that the entire spinal cord was ...

A. No, it wasn't there; there were only a couple of sections, which contained ...

Q. And that's a perfectly normal thing to happen when you remove the brain?

A. Yes.

Q. And then he says:

"There is no evidence of inflammation, haemorrhage or malformation."

A. Yes, I agree.

Q. "In particular, there is no evidence of central pontine myelinolysis, a destructive lesion which may occur following hyponatraemia with rapid correction."

A. Yes.

Q. So although you couldn't see hyponatraemia, the efforts to deal with hyponatraemia, if addressed over-zealously, may produce some reaction that you could see in the pathology?

A. Yes, this is a very well-known syndrome. It's quite unusual, but one may see this change where the myelin sheath, which is the wrapping around the nerve fibres themselves to increase their speed and efficiency, may break down. But it probably takes a few days to occur and one usually only sees it in cases where there has been an event which changes the serum sodium rapidly and the patient then survives for some days or weeks.

Q. That's not a situation like Claire?

A. No.

Q. And in any event you didn't see it?

A. No.

Q. Then on the next page, 360, he gives his opinion. He says:

"There is no evidence of acquired infection, meningitis or encephalitis."

A. I agree.

Q. "The cause of death, as given on the death certificate and in the inquest verdict, remains, in my opinion, not concordant with my observations."

Can we just pause there because that was one of the things that I was going to ask you about? Let's pull up the first page of the verdict on inquest. 091-002-002. Then if we have next to it the reference for the death certificate, which is 091-012-077. There we are.

So first in time is the death certificate:

"1(a), cerebral oedema; (b) status epilepticus."

And then if we look to the verdict:

"1(a) cerebral oedema due to meningoencephalitis, hyponatraemia due to excess ADH production and status epilepticus."

And he says that those two things do not accord with his observations. Do you agree with him about that?

A. I agree that the cerebral oedema is there, but I don't agree that there's meningoencephalitis. I think those are the two things that we can really comment on as pathologists.

Q. I think when you, in your report, were commenting on the cause of death, I think you did say that you weren't in agreement, as you just have now, with the verdict on inquest, but you were, I think, in agreement with the death certificate. Can you help us with that as to --
A. The death certificate on the right side of this screen here shows cerebral oedema, which there's no question about. That was there. Status epilepticus, again, we can't say very much as pathologists, but that's a clinical diagnosis.
Q. Ah.
THE CHAIRMAN: So when you say you agree with the death certificate, you agree with it to the extent that you're capable of contributing to it. So you agree with 1(a) and 1(b) is beyond your remit?
A. It's beyond my remit to say there was status epilepticus. Again, I would suggest there were subtle changes in the brain which might predispose to this, but I cannot directly speak to status epilepticus as a pathological finding.
MS ANYADIKE-DANES: So if it is there, you are deferring to the clinicians who formed that view?
A. Yes, indeed.
Q. But when it comes to the verdict on inquest, because there is a specific reference to something that you are

able to see and address in the pathology, you don't accept the meningoencephalitis?
A. That's correct.
Q. And if the meningoencephalitis had not been there, would you have had the same response to that verdict on inquest that you've just explained to the chairman in relation to the death certificate?
A. Yes, because we couldn't make any comment about the hyponatraemia either. We can simply say there's brain swelling.
Q. Thank you. So if we pull back 096-027-360 and have alongside it 361, so this is now the final part of Professor Harding's report. When he goes through with his conclusions, he says:
"The only relevant observation, albeit macroscopic, [in other words, with the naked eye] is of brain swelling."
And he judges that by:
"The excessive brain weight and also the effacement of gyri and the uncal prominence."
But then he says:
"These are rather weak indicators, not supported by a major downward shift of the brain and cerebellum, which is common in severely swollen brains and by the microscopy."

As far as you understand it, can you explain what he means there and, when you have done that, whether you agree with it?
A. As far as I can make out from his report, he's saying there is effacement of gyri and the uncal prominence. Effacement of gyri is when the normal folds of the brain become flattened because they're pushed up against the inside of the skull. Uncal prominence is when there is swelling of the medial parts of the brain close to the hippocampus, which again is another visual appearance, which would be suggestive of swelling. But as he says, they're rather weak indicators. He says:
"It's not supported by a major downward shift of the brain and cerebellum, which is common in severely swollen brains."
Again, it is a shame that we don't have any pictures of the brain to show if there was downward shift. But I think as I've mentioned before, there was a small amount of cerebellum adjacent to the upper cervical spinal cord, which would be consistent with some downward shift.
THE CHAIRMAN: I think he's talking about major downward shift; you're talking about some downward shift. So it's a question of degree, isn't it?
A. They would usually go together, but we're using some

very loose terms here. It's extremely difficult to be precise.
THE CHAIRMAN: Okay.
A. He also talks about lack of vacuolation in the white matter. In fact, I think there was some vacuolation in the white matter, but that can also occur when there has been lack of oxygen supply to the brain -- it's a very non-specific finding, very subjective -- which is why I have cited a paper by somebody called Houseman, who said all of these things are so difficult to assess, why don't we just weigh the brain and that will tell us whether it's swollen or not.
MS ANYADIKE-DANES: So it seems the upshot of what he is saying is that there was a very swollen brain, but he's not entirely clear from -- maybe you can interpret it for us -- whether what he is saying is that the actual evidence of that swollen brain ended up with the downward shift and coning that is being described. He seems not sure that he, as a pathologist, has seen the evidence of that.
A. That's correct. He's got a description, naked-eye description. He's also got a weight, which is very objective and it's much higher than the normal weight, but of course we have to consider that there are some children who have learning disabilities who will have

big brains and big heads. And so it's important that we know that she did or didn't have a big head so that we can judge whether or not she would have been expected to have a big brain. She might have had a heavier brain all her life, so he's saying it would have been helpful to have the head circumference to know whether she had a big brain or a big head. So that's one of his difficulties in assessing just brain weight.

But I think his conclusion is that the weight suggests it's big, there are soft signs here in the description to suggest it's swollen and during the terminal illness. Again, I'm pleased to see this, he refers to the CT scan, which is a very good check to show what was happening in life. That indicated the brain was swollen then as well.

Q. Is one way of interpreting what he's saying under paragraph 1 that he's actually dealing with the limitations of the evidence that has been provided to him?

A. Yes.

Q. Thank you. Or is available now for subsequent pathologists to view --

A. Yes.

Q. -- which doesn't necessarily mean that there wasn't sufficient cerebral oedema to lead to coning. Is one

way of looking at what he is saying to say that he, as a pathologist, hasn't actually seen that?

A. And the description he has seen doesn't lead him to be able to make any more certain statement, otherwise there's a brain swelling observed with the naked eye and a heavy brain and a CT scan.

Q. So then he says on his second point that what is obvious is that there's no information regarding the other internal organs, which might help us, for example, to exclude a cardiac cause of sudden death. If there had been a cardiac cause of sudden death, would one not see the footprints of that somewhere else, loss of oxygen to the brain or something of that sort?

A. Loss of oxygen to the brain is very non-specific and again maybe he would have seen some cardiac infarction. Mostly, these cardiac causes are identified in life by doing an ECG and recording the electrical activity of the heart. But I think it's a valid point that if you don't look, you're not going to find other causes.

Q. But is not part of the difficulty that, from the pathologist's point of view, there actually isn't very much hard evidence that you can produce as to the actual cause of her death?

A. The brain swelling is what we have.

Q. Yes, but the reason why the brain might have swollen.

A. No. There's not very much there. If there had been a rampant meningitis or meningoencephalitis, that would have been very helpful, but a very low grade one doesn't help us either way.

Q. Thank you. Then he goes on to 3, which is a point you have made:

"If cerebral oedema is present, then we require a cause of it. The inquest records 'meningoencephalitis and hyponatraemia due to excess ADH production and status epilepticus'. I consider the meningoencephalitis excluded both by microbiology [that would be his interpretation of the cerebrospinal fluid I presume] and the post-mortem neuropathology."

That's the work that he has done --

A. Yes.

Q. -- or the consideration that he has given to the slides produced by Doctors Mirakhur and Herron. Then he says:

"Hyponatraemia has been identified from the chemical pathology data."

Do you know what he means by that?

A. I think the lab tests, the blood tests --

Q. Just the serum sodium results?

A. That's right.

Q. "There is a history of vomiting which, when severe, may result in electrolyte disturbance. Hyponatraemia is

known to cause brain swelling, but there is no other specific neuropathological indicator for hyponatraemia that I am aware of."

A. I would agree, apart from the potential for myelinolysis if it's very rapidly treated and if the patient survives sufficiently long for that to be --

Q. But he has excluded that --

A. Yes.

Q. -- he is not finding it, and you had agreed with that exclusion because you didn't see it either.

A. Yes.

Q. And then he goes on to say that:

"The child was said to suffer from seizures. None were witnessed prior to hospital admission, certainly not [he says] status epilepticus. Moreover, the neuropathological sequelae of status were not present, nor was there damage to the hippocampus, which may be seen in children with chronic epilepsy."

If I pause there. The evidence is not entirely clear as to what has been described in terms of her presentation before she was admitted. Dr Webb's view is that either before or at the time of her admission that he has had a description that allowed him to take the view that she had suffered a convulsive seizure on the Monday. But leaving that aside, he ends up by

saying:

"There wasn't damage to the hippocampus, which may be seen in children with chronic epilepsy."

Now, you have a slightly different view?

A. I have a slightly different view because I've done more stains, and if he has had a chance to see those stains he might well have a different view himself. On the H&E stains, it wasn't obvious and it required special stains to point out that subtle change in the hippocampus.

Q. That's the very point I was going to ask you. If he was confining himself to the H&E stains, which he was, that really was quite subtle and maybe something there might be a difference of view as to whether that actually demonstrates that or indicates that?

A. Yes, absolutely.

Q. But it becomes clearer to you when you apply the special stains?

A. Yes.

MS ANYADIKE-DANES: Mr Chairman, I don't have any further questions for Dr Squier, but I was going to ask if I might have a few minutes to see if anybody else has.

THE CHAIRMAN: Yes. Before you do: doctor, the pathology team in Belfast in 1996 seems really to have been a team of three. There's Professor Dame Allen -- can I take it that you know her personally or just of her reputation?

A. I have met her on several occasions.

THE CHAIRMAN: Would it be fair to say she was one of the leading pathologists in the UK in the 80s and 90s?

A. Absolutely, yes.

THE CHAIRMAN: And did you know Dr Mirakhur?

A. I've only very recently -- no, a couple of years ago I met her because she was the treasurer of the Neuropathology Society, so I've met her in that capacity.

THE CHAIRMAN: In 1996, Dr Herron was a senior registrar, so he'd been there for some time, but beyond that team of three, there were occasional trainees, but at that time nobody else permanently there. Would that have been a team, particularly under the leadership of Professor Allen, of some repute and some standing?

A. Yes.

THE CHAIRMAN: The impression given is that it was also a team under constant and considerable pressure. I don't know if you can comment on that directly, but would that be unusual with pathologists?

A. I don't know what their workload was, but we have to remember that we're dealing with autopsy pathology here, which is often, in terms of the amount of work and the number of samples, quite a big burden. But on top of that, the priority is usually given to looking at brain

tumours in patients who come in for surgery and we need to make a diagnosis on those people so we can treat them appropriately. And that's always a top priority.

THE CHAIRMAN: And other forms of biopsies?

A. Yes. Mostly brain. That's one that really is critical and often has to be done at the time the patient is being operated on, and that's the one that pathologists really need to get right. So that's always the first priority in a neuropathology department.

THE CHAIRMAN: And one of the themes of their evidence, both Dr Mirakhur and Dr Herron, was that in an ideal world they would be able to spend more time looking through medical notes and records, not just relying on the autopsy request form, but there weren't many days when they lived in the ideal world. Would that be consistent with your experience?

A. I think so, and I think the point that I made this morning, that didn't really come across, that often you're doing this in an environment where technicians are saying, "Come on, we want to get this work done". So you're faced with technicians needing to finish the autopsy and move on, and you have a big pile of notes to read and it is very easy to say, "Well, we have a summary here, I'll take the brain out and then we'll go and read it all carefully in the cold light of day when

I have time to go back to my room and do it".

THE CHAIRMAN: Dr Herron said that the autopsy request form, which he received, was rather more detailed than the type of form that he very often receives, and certainly more detailed than one you'd receive for a coroner's post-mortem. Having seen the autopsy request form in Claire's case, would that be fuller than you would expect in your setting?

A. Yes. I think he's absolutely right there. I very often get brains sent to me with perhaps a name, an age and "history of epilepsy" or something and I have to fight very hard to get clinicians -- these are often from hospitals outside, but I have to make quite an effort to get more information.

THE CHAIRMAN: Is it a paradoxical result of that possibly that when you get a fuller request form than normal, then that might lead you to focus more on what's in that request form, particularly if you're under pressure, than going back through the medical notes and records because someone has taken the trouble, whether perfectly or otherwise, to give you more information than you normally get?

A. I think one has to be very carefully. I think, ideally, one should always look at the notes because you're never quite sure who's written that request form, particularly

if it is coming from another hospital. So one has to be careful. It can be difficult to get the case notes anyway if the patient's died in another hospital.

THE CHAIRMAN: Right. But in this case it was within the same hospital and it was from a consultant paediatrician of some standing.

A. I think he would very understandably rely on that form to do the autopsy. I would expect him to have the notes at a later stage to look at in more detail when he comes to formulating the final diagnosis.

THE CHAIRMAN: Okay. Thank you very much. I'll rise for a few minutes to see if you can sort out any further questioning.

MS ANYADIKE-DANES: Thank you.

(2.45 pm)

(A short break)

(2.52 pm)

MS ANYADIKE-DANES: Mr Chairman, just a couple of questions, one of which comes from one of your reports, Dr Squier. Can we please pull up 236-004-014. If you look at 68(b), the question there:

"If the underlying cause of that state was encephalitis, would changes be inevitable given the time course?"

And then you answer:

"Very rapidly progressive infectious encephalitis may cause death with little change in the brain. It is likely that Claire would have been predisposed to suffer from seizures early in any infectious or pyrexial illness due to her previous history and the hippocampal damage."

Are you able to explain what you mean there?

A. I think this is material that we've already perhaps covered, that as I've said before, a very rapidly progressive infectious disease may not cause reactive changes that we can see under the microscope in the brain. If Claire had had an infectious disease or a temperature, she may have been more likely than a normal child to have seizures because she had a predisposition to having epilepsy.

Q. And you can take it no further than that?

A. No.

Q. Then could I ask you to look at 236-004-017? Do you see just immediately under the question at 75:

"What is/are the most likely underlying causes of Claire's condition given your findings and the post-mortem findings?"

And you say:

"The most likely cause is an epilepsy syndrome. The nature of a syndrome which would account for both

Claire's epileptic seizures and her developmental delay should be addressed by a paediatric neurologist with experience in these complex genetic syndromes. Her terminal illness appears to have been epileptic activity precipitated by a concurrent infection and complicated by hyponatraemia."

The question is: what is the evidence for that view that you express there?

A. The evidence for the epileptic activity is purely based on the clinical description of what was thought to be non-convulsive status epilepticus, and I defer entirely to the clinicians and the clinical paediatric neurologists as to whether that was or was not established. The infection suggestion comes from, again, the clinical suggestion that she had an encephalitis. We don't find any evidence for it, but she may well have had a systemic infection, and again I defer to the clinicians and the microbiologists for their interpretation of the blood tests and the CSF findings.

Q. Thank you. And I take it that the complication by hyponatraemia is another matter which you would defer to the interpretation of her condition or her presentation together with the results of her blood tests in terms of serum sodium levels?

A. Yes, that's for the chemical pathologists again.

Q. Thank you. Then finally, for my part, you have described the number of brains you typically expect to see during the year and you've talked about your research and so forth. If you can take yourself back to 1996 for a moment, how much of your time was spent literally looking at brains or brain tissue through the microscope or with your naked eye, that kind of examination?

A. During 1996 how much time was spent?

Q. I'm not asking you to specifically remember 1996, but in the mid-1990s.

A. Oh, 70, 80 per cent of my day would be spent either looking at brains or looking down a microscope.

MS ANYADIKE-DANES: Thank you. Mr Chairman, I don't have anything more, but I think --

MR McCREA: There's just one matter which is not really a question, but is more comment.

At the start of the evidence that was given this morning, at the start of the issue as to whether or not Dr Squier should give the evidence, the family considered it inappropriate to make any comment as to whether or not Dr Squier should or should not give evidence. However, now that she has given evidence, the family want simply to say a very brief comment.

They consider that the doctor's evidence -- her written evidence and her oral evidence -- to be given in a very fair, very balanced manner. They also instructed me to indicate to the inquiry that the evidence that has been given has assisted them greatly in understanding what did and, in fact, did not happen to their daughter. So in that sense, it has been very positive from their point of view.

THE CHAIRMAN: Okay. Thank you very much. To be fair to the Trust, if there is criticism of an expert who's retained at an inquiry or something like that, it's not unreasonable for the Trust to raise the issue. And the Trust was never suggesting that we should not have an expert pathologist witness.

The Trust was querying the continued retention of Dr Squier -- not so much after the divide about shaken babies emerged, but specifically after it emerged that there had been a complaint to the GMC. Is that the gist of it, Mr McAlinden? So in fact, what the Trust was suggesting, as you may have seen in the letters, was we frankly dispense with Dr Squier and retain a replacement expert.

If I had acceded to the Trust's request, it would not have meant that there would not have been an expert witness and hopefully any alternative expert witness

would have been as of significant assistance as Dr Squier has been, but I take the point. I presume that anyone who wants to can come back in submissions on that at a later course.

Thank you very much, doctor. That brings to an end your evidence. I understand you're going to stay and listen to Professor Harding in any event.

A. If I may.

THE CHAIRMAN: Of course you may. We'll break for a few minutes.

(The witness withdrew)

We're hoping to get the video link set up in the next few minutes and we'll start at 3.05, or so, whenever the link is up. It would be helpful if everybody could leave the chamber for the next few minutes so that we can arrange the screen and for the test to be carried out. Thank you very much.

(2.58 pm)

(A short break)

(3.17 pm)

PROFESSOR BRIAN HARDING (called)

(The witness appeared via video link)

THE CHAIRMAN: Professor Harding, can you hear me in Banbridge?

A. Yes, I can.

THE CHAIRMAN: My name is O'Hara, I am the chairman of the inquiry. You are going to be asked questions, in a few moments, by Ms Anyadike-Danes arising from various issues, which I think you are broadly familiar with. But before we do that, can I ask you to take the oath or affirm?

Questions from MS ANYADIKE-DANES

MS ANYADIKE-DANES: Professor, good morning.

A. Good morning.

Q. Professor, do you have a copy of your curriculum vitae there?

A. I do not, but I asked your assistant to get in touch with my assistant in Philadelphia to send it to you. Has it not --

Q. We have it. I will just ask a few questions from it.

A. Of course.

Q. Can I ask you: you were originally engaged on behalf of the Police Service of Northern Ireland, PSNI, to carry out a report.

A. I was asked to carry out a report. I cannot remember who it was by, whether it was the police service or your inquiry. But I did do a report back in, I think, 2004.

Q. I think it was 2007.

A. Yes.

Q. Not to be pulled up, but we have the reference for it,

096-027-357 and it's dated 22 August 2007. It's about four pages; do you recall that?

A. Yes.

Q. And then you provided a very short report, a one-page report, for the inquiry on 24 March 2011. We don't need to pull that up either, but it's 235-002-001.

A. Yes.

Q. Do you recall that?

A. Yes.

Q. Since then, we have provided you with a number of documents. You will have seen obviously the autopsy report, which you saw originally, the witness statements from the pathologists, Dr Mirakhur and Dr Herron.

A. Yes.

Q. And you will have seen the reports from the inquiry's own neuropathology expert, who is Dr Squier.

A. Yes.

Q. And in her report, she has provided some photographs of the stains that she prepared and also included the photographs of the stains that were prepared by Doctors Herron and Mirakhur, which you originally saw, and you have seen all that material.

A. Yes, I have.

Q. Doctors Herron and Mirakhur gave evidence last week and there is a transcript. That was sent to you, but

I don't know if you have had an opportunity to look at it.

A. I had a brief opportunity to look at it because I think I only got it this morning when it was very early.

Q. I understand.

A. But I have it here.

Q. Thank you very much indeed. Do you have access to at least the photographs of the stains that are included with Dr Squier's report?

A. I think so. It may take me a moment to find them, but yes, I do.

Q. At some point in time, I'm going to ask you to look those up because I'm going to ask you to comment on them.

A. Right.

Q. In relation to the two reports that you have provided, subject to anything else that you may say in this oral hearing, do you adopt that as your evidence on the pathology?

A. Yes.

Q. Thank you. I wonder then if I can ask you a little bit about your curriculum vitae. The reference that we have given it is 311-040-001. We can see that you did your postgraduate training, you started as a house officer in St. James's Hospital, Balham. Then, in the latter

parts, as a senior registrar, you were at St George's Hospital in London and also the National Hospital for Neurology and Neurosurgery in Queen's Square, London.

A. That's right.

Q. That takes you up to 1983. You also had university appointments. In fact, at the time when you were providing the report for the PSNI, which spans 1994 to 2008, you were an honorary senior lecturer at the Institute of Neurology at the University of London.

A. Yes. That was my academic hat, but I was consultant at Great Ormond Street from 1983, I think.

Q. Yes. Currently, you are the professor of pathology and laboratory medicine at the Children's Hospital of Philadelphia and the University of Pennsylvania School of Medicine.

A. That's right.

Q. And you have been that since 2009?

A. Yes.

Q. In terms of your hospital and administrative appointments, again at the time when you were asked to provide the report to the PSNI, but also at the time of Claire's admission in 1996, you were a consultant neuropathologist at Great Ormond Street Hospital.

A. That's right, yes.

Q. And you first became a consultant at that hospital in

1994.

A. Well, I was jointly consultant at that hospital and Queen's Square, which is now called the National Hospital for Neurosurgery and Neurology in 1983. Then they switched my contract, so I was full-time at Great Ormond Street in the 1990s. So I continued to be consultant at Great Ormond Street in effect from 1983 until I relinquished that job at the end of 2008.

Q. So in fact, you have been a consultant associated with the Great Ormond Street Hospital from 1983 until, effectively, you left to take up your position in Philadelphia?

A. That's correct, yes.

Q. You were a member of the Royal College of Pathologists in neuropathology?

A. Yes.

Q. And I won't go through all your membership of professional and scientific societies. It's to be shown there at 002 of your curriculum vitae.

If you would, could you summarise, at the time of 1996 -- which is when Claire was admitted -- and at the time when you were asked to provide the report to the PSNI -- which was in 2007 -- what were your main research interests? If we start with 1996.

A. My main research interests surrounded paediatric

neuropathology, particularly metabolic and degenerative disorders and rare disorders of children and malformations of childhood, which -- I was more interested in that than in tumours, though I did tumours every day as part of my clinical work. Those were my main interests spanning most of my career.

Q. I see. In particular, were there any specific areas within that that you were interested in and developed expertise in?

A. Well, as the only full-time paediatric neuropathologist in Great Britain, I got a lot of very interesting rare metabolic disorders to examine, and I became very interested, particularly in some diseases which are now known to be mitochondrial. They weren't when I started, we only guessed. Things like Alpers-Huttenlocher's disease and Leigh's disease and things like this. Rather degenerative diseases of the brain in children, and young children at that, which we now know the aetiology of. So I saw a lot of that. I also saw a lot of malformations, developmental anomalies of the brain which some children are born with, because that is also part of the remit of a paediatric neuropathologist. Some of these are rare and so we got both tertiary and quaternary referrals.

Q. And epilepsy, would that be an area that you --

A. I did a lot of epilepsy, a lot of epilepsy, because we -- Great Ormond Street has the largest epilepsy surgery service in Great Britain and one of the largest in Europe. So there was a lot of epilepsy surgery going on and I was, for many years, the sole neuropathologist working in that department until I trained up a successor, who's now running the department. So I saw a lot of epilepsy cases, yes. But surgical epilepsy, rather than cases coming to autopsy, although we did see some cases that came to autopsy following severe seizures. But seizures are the result of so many different things that you can't, you know, generalise.

Q. I understand. Can I then ask you some more specific questions that relate to this particular case?

I'd like to start first with the question of stains. The slides that you saw and examined in 2007, those were the slides that had been provided to you that had been prepared by the pathologists in the case, Doctors Herron and Mirakhur; is that correct?

A. That's correct, yes.

Q. Before I go to what sorts of stains -- maybe I will start with that way first in the light of the evidence from Dr Squier.

What sort of stains were used on those slides?

A. As I recall, they were the standard first-line stain

that all pathologists use, haematoxylin and eosin, which is a very good --

Q. H&E?

A. H&E, yes. The reason why it's used as the first line is because it is an excellent stain for showing the generalities of pathology and anatomy. So it's a very good all-round stain to start with and everybody these days still starts with that stain or maybe finishes with that stain, but that's the first thing we do.

Q. Then it may be that you will go on and apply more specialist stains, depending on what you do and don't see and what you're interested in?

A. That's right, yes. Exactly.

Q. Those slides would have been prepared in 1997, probably, because the autopsy was carried out in the October of 1996 and then the brain would be fixing and so forth. So they would have probably been prepared some time in the early part of 1997. You're looking at them for the purposes of your report in about 2007. Is there any --

A. Yes.

Q. Is there any concern that the quality of them degrades so that your analysis or assessment of what they're showing is compromised in any way?

A. Well, they didn't appear to have degraded when I saw them, as I would have commented on that. Generally

speaking, no, if they're properly prepared and mounted, so there's enough mounting medium underneath the cover slip and they're stored properly, they should be perfectly all right for a long time. This is not a stain that -- the stain is not one that tends to fade. There are stains that fade and we're well aware of that, but this one doesn't fade and, as I say, as far as I know, the slides were in a reasonable condition. I had no complaint about the slides that I received. I would have stated in my report if I felt they were compromised in any way.

Q. If they do fade slightly, are you able to do anything about that?

A. Oh yes. You can, what you can do, if you have the patience, is to get the cover slip off, but that requires a solvent and sometimes you have to wait for the solvent to work. They you lift the cover slip -- that's the top piece of glass -- off and they you are left with the slide with the stained section underneath and you can restain the section, you can take the stain out and restain it. That stain is like a -- they're dyes, those particular stains. So you can restain the section. And I have done that in the past with my own slides, if they've been -- things in our department that are very ancient and they've dried out.

The problem is if they don't put enough mountant in, the mountant can dry out and that can let air in and that interferes with the section. But those sections did not need repairing in any way, as far as I can recall. If they had, I wouldn't have been able to issue a report.

Q. Thank you. In terms of any further specialist stains, Dr Squier said in one of her reports -- and the reference is 236-007-005 -- she thought there was a lack of hippocampal pathology due to the apparent failure of the pathologist to apply what she regarded as special stains to look for subtle hippocampal pathology to explain the history of epilepsy or confirm the findings thought to represent neuronal migration disorder. If we pause there for the moment, the evidence she has given today is when she looked at those slides with the H&E stains, she wasn't entirely sure that she hadn't seen something that might be a little suggestive of perhaps some scarring, bearing in mind Claire's history of epilepsy. And she said she did apply further stains to see if she could highlight that and see what was disclosed there. And as a result of that, she said she did see evidence of a little scarring and she has described that as you probably recall in her report.

She fairly said that it might not be immediately apparent on the H&E stains, but she was looking in particular because of the query over whether anything could be done to explain the developmental delay of Claire and her epileptic history. You have seen what she says about that. Do you have a view about what she saw and the differences between that and you?

A. Well, I think ... I perfectly understand her position and I think that if she had some question marks over what she saw on the H&E, it was quite correct of her to take it further. I didn't have any question marks over what I saw on the H&E, so when I examined the sections, which was before her, I think, I didn't feel it was necessary to take it further.

Subtle gliosis, as she describes in the hippocampus -- it's very subtle. I've seen her extra stain, the GFAP, at least the picture of it. It's very subtle and often you see this in normal -- apparently normal people. So I'd like to have a little bit more evidence from the H&E before I rely on the special stains. There are cases where you will find things that you don't see on the H&E, I perfectly agree. But in this situation, at the time I examined the sections, I didn't feel that there were sufficient grounds to ask for the blocks and to take more or ask for more

sections.

I certainly understand her reasoning; that is the normal reasoning for a pathologist: if you feel that there's another question to answer, then take it further -- or if there's a major question from outside.

But when I examined them, I didn't think that this was sufficient evidence on the H&E for both things, the question of the migration defect and the question of the hippocampus.

Q. In relation to the query over whether there was viral encephalitis, she said that she didn't see it on the H&E, but because it was a specific query, she applied -- well, essentially what she said, I'm not quoting her verbatim -- some further stains to see if that might highlight things that might identify what she had failed it to see on the H&E. The upshot was she still didn't really see anything there that would allow her to form the view that there was evidence of viral encephalitis. Do you appreciate the application of further stains just to check if there was anything there?

A. Yes, I do. But I note that she still came to the conclusion that I came to on the H&E. I think one must be very cautious with these markers because you have to put everything into a global concept. So I expect to see, particularly with things like encephalitis,

something definite on the H&E before I will jump to conclusions. I think subtle pathological changes are very tricky to discuss, very tricky to consider in these situations, and one can be too ready to accept these things unless you've got very definite evidence, I think. This has always been my view.

Q. Is it a prudent step to take given that one set of pathologists have believed they have seen that, and you not thinking that you do see it to then apply special stains --

A. I must confess, I think it is a prudent step and I think she was very reasonable to do it. At the time, I was quite happy with what I'd seen, but I think she was reasonably prudent, yes.

Q. Thank you.

Professor Lucas, who's a professor of histopathology, and he has been engaged by the inquiry to provide assistance on the general way in which autopsies are conducted, in his report -- I don't know whether you have seen it, but in the chamber --

A. No, I don't think so.

Q. -- the reference for it is 239-002-011, going on to 012. He expressed his surprise that:

"... no one had performed specific immunohistochemical stains on the tissue slides to

determine for sure the presence or absence of inflammatory T-cells or reactive astrocytes and microglia."

And:

"In [his] book, infiltrating CD8+ or T-cells are necessary to diagnose encephalitis in most cases and they're either there in the brain or they're not and if they're not, then it's not encephalitis."

Can you comment on that?

A. Well, I agree with him that there have to be infiltrating T-cells in the brain, infiltrating chronic inflammatory cells in the brain for there to be encephalitis. Whether it's necessary to do all the markers -- I mean, he's taken it even further than Dr Squier. This is his opinion. I think that one needs to start from a baseline and the baseline was the H&E and it wasn't there. But I can see that in this situation where there's some argument between the clinical and the pathological positions, it probably would be useful to look at that. I think that Dr Squier went reasonably far enough.

Q. Thank you. Then I'd like to ask you a little bit about the status epilepticus. My starting point is going to be the autopsy request form. Were you provided with a copy? You have seen a copy of that?

A. I may have done a long time -- I haven't recently, I don't know. If it was with the first bundle that I got, then yes. But I'm afraid it's a long time ago since I saw the original bundle.
Q. Not to worry, I can help you with it. For the chamber, it's 090-054-183 together with 184. I can help you with it. This is coming from the consultant paediatrician, her autopsy request form to the pathologist, telling them it's a brain only and this is the basic information that is provided.
A. Right.
Q. It's a standard form. You may well have seen something similar when you were working at Great Ormond Street. The way this is structured is that there is a bit of clinical presentation, some history of present illness, past medical history. Under the "past medical history", it refers to "mental handicap" and "seizures from six months to four years".
A. Right.
Q. And then under the clinical diagnosis, it states:
"Cerebral oedema, secondary to status epilepticus."
Then there's:
"Query underlying encephalitis."
And then on the next page, which is also a standard form, it has a list of clinical problems in order of

importance and there are four spaces. I presume if you had more than four, you'd add those.
A. Right.
Q. First is cerebral oedema, second is status epilepticus, third is inappropriate ADH secretion. The fourth is again "query viral encephalitis".
A. Right.
Q. What the pathologists say they were doing is they were looking to see if there's anything structural in the brain, any structural abnormality, a lesion, anything like that, that might assist with the mental handicap or the seizures from six months to four years. Then they were looking to see what they could do within the constraints of the pathology, what they could do to assist with those four clinical problems, the cerebral oedema, status epilepticus, inappropriate ADH and the query of the viral encephalitis.
In some respects, you have dealt with those four points in your report for the PSNI, not necessarily in that way, but you've touched upon the evidence that you saw and how that bears on those problems, and one particular aspect you looked at for us. So I'm going to ask you about your evidence in relation to that and why it differs from what the pathologists found and to the extent that it differs or agrees with the report of

Dr Squier.
A. Right.
Q. So if we start with the status epilepticus. Can you help as to what assistance you would think, as a pathologist, you could offer on that particular problem?
A. Status epilepticus is a clinical description of a very severe seizural event. Sometimes we don't see any evidence in the brain that status epilepticus has occurred unless there is damage due to the lack of oxygen, hypoxia, or a metabolic insult to the brain when it's undergoing these very severe seizures. We would look for, as you touched on, lesions in the brain that might lead to seizures or damage to the hippocampus, either following seizures or resulting from seizures. This is a complex area in relation to seizural activity, but in many cases of status epilepticus, you find very little in the brain to account for the clinical scenario. Does that answer your question?
Q. Yes, it does. I wonder if you could help us in this way: what Dr Squier's evidence was -- she agrees with you that she doesn't think that you are going to find evidence of status epilepticus per se, you might find evidence of any damage that was done as a result of the prolonged seizure activity. Alternatively, you might

find something that had predisposed the brain to respond in that way.
A. Yes.
Q. That's the sort of thing that she was looking for.
A. Yes.
Q. And she was particularly looking in the hippocampus, which is the area that she thought was likely to be most conducive to seeing that evidence, to see if she could see anything there.
A. Yes.
Q. And she said that she couldn't particularly see very much on the H&E, and this is when she applied her GFAP stains to see what that would disclose. You may have seen -- I don't know if you can pull it up there. Can you pull up there a reference 236-007-022?
A. Yes.
Q. It should be a set of four brown-ish, to my eyes --
A. Yes. They are brown.
Q. The two at the top are the stains in relation to Claire and the two at the bottom are the stains in a person that she referred to as the control, which is a 10 year-old male who died with no history of epilepsy. The right-hand side is a magnification of the left-hand side, I believe. And she was explaining that those darker dots that one sees towards the arrow and going 1,

2, 3, and maybe 4 diagonally downwards towards the right-hand side, that was very subtle scarring that she saw when she applied the stains. She thought that that might be some evidence of perhaps Claire's previous epileptic history, and if there was some evidence like that, that might indicate what was already thought to be the case, which was that she was a child who was vulnerable to something perhaps triggering further seizures later on. Do you interpret that in that way?

A. No, I don't. I think that -- there isn't a lot of difference between the control. I'm looking at a corner of the pictures that she has taken. Although they're very good pictures, I don't think there's a lot of difference between the control and the patient. The problem is that you often do see a certain amount of gliosis in this area. On its own, I don't consider it enough to build hypothesis upon hypothesis and say that this is evidence of ... If there was a very ... I can't recall how severe Claire's seizural history was, leaving aside the last status epilepticus.

In many cases, we see sudden death in epilepsy. That is regularly seen by pathologists because those cases have to come to autopsy. And these are patients who have had seizures on and off for years and, sadly, suddenly die and you find very little in their

hippocampus. So to base anything on this very subtle, questionable gliosis, I think, is not safe, shall we say, as a diagnosis. I would expect to see, in somebody who had severe seizures and damage to the hippocampus, neuronal loss in some parts of the hippocampal structure first with the gliosis, the scarring, that comes on top of it, and that wasn't here. The main neuronal architecture of the hippocampus was intact in the section I saw. So that would be the first line of damage, generally speaking, and that wasn't present and Dr Squier didn't find it either. So I find this subtle gliosis a little bit too little to make very much of.

Q. So if there's any subtle gliosis there, then it's not enough to produce the kinds of effects that people were looking for, if I can put it that way?

A. No, exactly.

Q. So it might be there, but if it is, it's not necessarily significant in predisposing her or triggering her non-fitting status that she experienced much later on --

A. Exactly.

Q. -- when she was 9 years old?

A. This is the failure of neuropathology: we don't necessarily have the tools yet to see, at the synaptic level, why some idiopathic epilepsy occurs. If there's a lesion, if there's a tumour, if there is major damage

at birth, which damages the hippocampus through hypoxia, that can then trigger epilepsy, and we know all about that. But there are many cases where we still don't see structurally at the level we look at anything to ascribe the epilepsy to.

Q. Does that mean that's just the level that the science has got to?

A. Yes.

Q. There may be something, but the tools you have don't allow you to either see it or interpret in that way?

A. Right. Yes, there may be biochemical and sub-cellular changes which we can't address at the moment. At least not through this method, yes. And there are genetic causes of epilepsy that we are now finding or our colleagues are now finding, and these patients, some of them, undergo epilepsy surgery and I see the tissue and I see the hippocampus and there's not much damage, but they definitely have sub-cellular defects, like defects in the channels which allow the sodium and potassium and calcium ions to move through the cell membranes. These are known, the genetics of these conditions are known, but they don't necessarily produce very obvious structural changes in the brain that a neuropathologist can find.

Q. If I can ask you on the neuronal migration disorder.

I think Dr Squier has formed the view that if there was any, it was so subtle that she couldn't see it. Dr Mirakhur and Dr Herron have fairly said that they are talking about something subtle, and I think their view is it comes down to a matter of interpretation. I wonder if I can put up the image which they were all looking at to try and explain to the inquiry why they either think it's there or they don't think it's there. I hope you have it there. It's 236-007-040.

A. Isn't it in Dr Squier's report as well?

Q. Yes.

A. That's the quickest way to find it. I'll do that.

Q. In hers, it's called "image 10".

A. Right. She's given you a little digest about neuronal migration --

Q. Yes.

A. -- then image 10, yes. There are arrows to the cells that they are calling migration disorder. And on the right-hand side in her picture she has shown what she thinks is a migration disorder.

Q. I think that's the wrong one. That's in her presentation. If you carry on down, I see where you are.

A. Yes, I see. The original ones are at the bottom. Yes. I'm getting there.

Q. Image 10.
A. Oh yes. I have it.
Q. Thank you.
A. On the left-hand side, there's a row of dense blue dots, which indicate the ventricular surface, and underneath, to the right-hand side, the way I look at it, there's a cluster of cells, which they obviously think are evidence of migration defect.
Q. Yes.
A. Yes.
Q. In fact, the way it's referred to in the autopsy report is -- it says:
"Focal collections of neurones are present, arranged in a rather haphazard manner."
I think one finds that at 090-003-004. So that's a description given of it. Both Dr Herron and Dr Mirakhur gave evidence. I think Dr Herron's view is that this is more the interpretation of Dr Mirakhur. It's not that he's resiling from it, just that was the way the work was divided out. And she has characterised this as the basis of her conclusion that there was a neuronal migration disorder. Admittedly, she considers it to be at the lower end of the range, if I can put it that way.
Can you help with that? Why don't you recognise

this as that?
A. Well, I think this is probably what we call an arrest of neuroblasts, rather primitive cells. They don't look like mature neurones and you often see rests like this around the ventricle in children. I think that's roughly what Dr Squier thought. This is within the normal range. If you want to see -- there are many sorts of neuronal migration defects and I've seen many over the 35 years I've been looking at these things. I've never seen one like this. This is not a neuronal migration defect. If there were mature neurones in sufficient number, clustered together, to form a little nodule, which usually protrudes, as you saw in Dr Squier's -- I have got a picture here. They protrude like little bumps into the ventricle. In a child of this age, Claire's age, 9, they are mature neurones, haphazardly arranged, sometimes trying to pretend that they are cerebral cortex. There are all sorts of possibilities. That is it a heterotopia -- heterotopus, in the wrong place -- and that might indicate neuronal migration defect. That picture does not.
Q. Professor Harding, if you go back to where you said that there were two arrows and you were looking at that before, I can give that reference here. In our referencing, it's 236-007-030.

A. Yes.
Q. Do you see that? There's the original slide on the left-hand side with two arrows pointing towards it.
A. Yes. The left-hand side is there, is Dr Mirakhur's picture, and on the right-hand side is Dr Squier's picture. That's much more like what you'd see. Only I have some even better pictures. But I don't know whether I can show them to you.
THE CHAIRMAN: Sorry, where --
A. This is a well-known --
THE CHAIRMAN: Professor, sorry, for one moment. When you say you have better pictures, do you have them available in front of you?
A. I can have them available. I don't know whether your camera -- I will try.
THE CHAIRMAN: Let's try that.
A. Give me a moment.
THE CHAIRMAN: If it doesn't work, it doesn't work. If you have a better example of neuronal migration disorder, let's see it.
A. Dr Squier's is perfectly all right. It's just that she took it from a very young child. I think it's a neonatal picture and I'm trying to find -- I sent it to myself yesterday. Here we are. I don't know whether this will work.

This is a slice of brain (indicating).
MS ANYADIKE-DANES: We can see that.
A. In the ventricle, do you see those bumps, like clusters of eggs?
THE CHAIRMAN: Where your left index finger was?
A. Let me make it bigger.
MS ANYADIKE-DANES: Yes.
A. Do you see that? This has been cut through. So you can see it's a coronal slice of brain. So you can see into the ventricle because it's not a thin slice, it's a thick slice. And you can see that these bumps in the floor -- and one of the bumps has been cut through, and you can see that.
THE CHAIRMAN: Professor, I'm not sure this is really working very well.
A. No, I wasn't sure it would. What I wanted to say was that -- because there's another picture there. Dr Squier's pictures are perfectly good, but they are of a much younger child, whereas Claire was 9 and the pictures I was showing you were from a child who I recently examined, who was 9 months. And in that 9 months child there were a lot of those bumps and the cells inside them were mature nerve cells and very obvious. So this to me is not -- I'm afraid it's a normal variant and so often one gets sent things like

this by people who are not so expert at looking at heterotopias and that is all I would say.

THE CHAIRMAN: Professor, can I put it to you this way: Dr Squier gave evidence earlier this afternoon, our time -- this morning, your time -- and she said looking at this particular slide, that she did not interpret that slide to show neuronal migration disorder. She said it looked perfectly normal to her and, in fact, that there was nowhere near sufficient of a cluster for her to regard it as abnormal.

A. Exactly.

THE CHAIRMAN: Do you agree with that?

A. That's what I've been saying in terms, yes. And they are not mature enough. It's just no way a migration disorder.

THE CHAIRMAN: Thank you.

MS ANYADIKE-DANES: Then I wonder if I could ask you about the encephalitis because that's the other finding that the pathologists said they saw evidence of and which neither you nor Dr Squier really think there is evidence of. If you can stick with the slides of Dr Mirakhur, it's the first in the series of the slides, not the slice through, the first in the series. In ours it's called "image 2". If you can use Dr Squier's references, it'll be 236-007-032. It's the one with the

large blood vessel in the middle.

A. Yes.

Q. This is one of the slides that Dr Herron and Dr Mirakhur relied upon as indicating evidence of some inflammatory response and therefore some evidence for encephalitis albeit that they considered it a low-grade sub-acute meningoencephalitis. But nonetheless, Dr Mirakhur was sure that they had seen something, it was just low grade. Dr Squier's evidence was that she didn't think that amounted to evidence of meningoencephalitis. Can you explain what you think is happening in that slide?

A. There are a few excess cells in the perivascular space, which you do sometimes see. But there is not an infiltration of the tissue around it to suggest that there's an encephalitis. There are no clusters of inflammatory cells in the grey matter of the brain around it. There was no evidence of nerve cells being attacked by inflammatory cells, which you see in an encephalitis, and I, like Dr Squier, did not consider this amounted to a definite inflammation of the brain.

In addition, where there is an encephalitis, there's also a meningeal infiltrate, and I didn't consider that the number of cells that I saw in the meninges were sufficient to call it a meningitis either. So in my

opinion, this wasn't evidence -- at least structural evidence -- for an inflammatory disorder.

Q. If you go to literally the next slide from that, so the next image that you have, that was the other image or slide, I should say, from which Dr Mirakhur and Dr Herron concluded that there was some evidence of an inflammatory response and allowed them to refer to a low-grade sub-acute meningoencephalitis. Can you describe what you see there and how you interpret it?

A. Well, I'm not clear where I am, whether this is the surface of a sulcus. Do they say where it is?

Q. Not entirely.

A. Because it might be the surface, in which case we're looking at the meninges. There may be a blood vessel in there, I'm not sure. There's a space and then there are some cells, some of which are probably chronic inflammatory cells, but they're very small numbers, it's very focal, and I just ... It's not the way I would diagnose a meningitis. I would want to see much more than this.

I would expect, actually, even in a mixed infiltrate, although this was three days, was it, between her --

Q. Yes.

A. There might still be acute cells. There aren't any

acute cells there. But if there was a meningitis, I would expect to see a much more florid reaction, much more widespread than just a little focus like this. We see these things all the time and we can't, if you like, in "normal" -- and we can't jump to conclusions too quickly.

Q. Although you say you would expect to see a much more florid reaction, is it nonetheless possible that this is actually evidence of just how the pathologists have described it: a low grade sub-acute meningoencephalitis?

A. On the evidence of what I saw at the time I looked at it, I wouldn't agree that it's a low-grade meningoencephalitis. That's all I can say.

THE CHAIRMAN: Okay. Professor, for completeness, Dr Herron said that, on a scale of 1 to 10, he would place this at 1 to 2. Dr Mirakhur would place it at 2. But Dr Mirakhur also said that in order for encephalitis to be identified as the contributory cause of Claire's death, this would need to be 5. So that just gives you some idea of just how low grade they are suggesting it is. Do I gather from your evidence that you don't even see it as being around 1 or 2?

A. Well, I ... With respect, I don't grade them. I either consider it's there or it isn't, with this sort of thing. I think it's very difficult to make a scale

here. I don't think it's there.

THE CHAIRMAN: Okay, thank you.

MS ANYADIKE-DANES: Thank you. Then I'm not sure if you're aware that the inquiry engaged a consultant microbiologist, Professor Cartwright, to provide advice, particularly on the cerebrospinal fluid. In fact, as a result of that advice we asked you a particular question that he wanted raised. That was about the acute fulminant and that came out of his concerns. He looked at the results of the CSF and was a little bit concerned about the level of it and what was shown. So he asked us to put that point to you. You've given your evidence on it. 235-002-001.

The question that arose out of his query to us is:

"Whether, in your experience, an acute and fulminant encephalitis causing cerebral oedema, coning and death in the space of three days could occur in the absence of clear neuropathological changes, possibly as a result of the rapidity of development of such an infection?"

And your answer is:

"Given the marked degree of brain swelling noted clinically and confirmed at post-mortem, I consider it extremely unlikely that microscopic evidence of encephalitis would not be evident by three days. I have seen it occurring within 36 hours."

A. Yes. Well, that's from my experience. Nobody has a large experience of seeing encephalitis in children, though I've seen a few cases. I remember distinctly this particular case where the child was rushed to hospital and died not very long afterwards. They had a clinical suspicion of encephalitis and, much to my surprise, there was, because there had been very little prodrome before the child got to hospital. And this was -- it may have even been less than 36 hours, but certainly very quick, and there was a very obvious encephalitis in the brainstem of this child. So that's what I would expect. I noted from Dr Squier's report that she quotes a paper, which brings up the possibility you may not see very much.

But what little experience I have is that I would expect, having seen that case and one or two others, to see something. Given the severe brain swelling and the degree of obtundation of the child, I would expect to see much more obvious evidence, provided the brain was blocked properly and they took enough ... And they did a reasonable survey, which I presume they did, I can't remember which blocks they took now because sometimes these things can be focal. But given the widespread brain swelling and so on, I would have expected to see something, yes.

Q. Is it possible that it wasn't sufficiently marked to cause the cerebral oedema in the way that it's framed in the question, but nonetheless is present, perhaps contributing to the general precipitating of a seizure in some way and that the cerebral oedema itself has an independent cause? So in other words, is it possible to have some evidence of encephalitis, which hasn't got into the brain yet, but it's there in the body, it's present, and the cerebral oedema, the fact that that is so marked, you can't, if you like, reflect that from the low level of encephalitis; is that possible?

A. I suppose it is possible. Anything is possible. It would be very difficult to dissect the two. But unless there's very definite evidence -- clinical evidence of encephalitis in this case -- I would be looking for another cause of the oedema.

Q. Then if I can put to you some queries that Professor Cartwright had when he gave evidence. He gave evidence on 7 November. One finds them at page 84. I've asked Dr Squier also the same issue. It starts at line 4:

"What I would hypothesise here, or the hypothesis that I would put to Professor Harding, would be: can you get a massive rise in intracranial pressure consequent upon cerebral oedema before you have had a chance for

white blood cells to migrate into the brain matter?"

Which is a much better way of saying what I was clumsily struggling to say. And then he goes on at line 13:

"What I am interested in is: can you exclude the possibility that you could have a failure of white blood cells to infiltrate the brain matter after a period of three days?"

A. Due to brain swelling?

Q. Yes. You see the way it's summed up at line 22:

"In an attempt to square the circle between yourself and Dr Harding, you're wondering if the cerebral oedema happened so quickly that the white blood cells didn't have a chance to get up to the brain, which would be the histopathological evidence he would see?"

That's you.

A. I can't accept that because there's no evidence here that blood -- I mean, he's saying that the white cells can't get to the brain, but then what about the rest of the blood? I mean, there wasn't that much hypoxic change in this brain. In other words, the blood supply -- in cases of brain death, which this wasn't, the blood supply to the brain stops and the brain sort of sits there and autolyses in situ. It's one of these things that neuropathologists dread because then we

can't do anything. We can't get a result. But that's a case where the blood flow to the brain stops. But here, the blood flow to the brain did not stop, viz there isn't evidence of brain destruction or hypoxic damage to the nerve cells. So I don't see how you could hypothesise that the white cells are not getting there, they're in the blood, and the blood is still getting to the brain in this case. So I don't see that as a hypothesis I could follow.

Q. What Dr Squier was positing was: was it possible to have some sort of overwhelming response, which happened so quickly that you wouldn't see the evidence of it in the brain?

A. Well ... Yes, but ... Perhaps. Where does that take you? That means you can't say anything.

Q. It means that either you can't say anything or something else may have caused -- well, I suppose then you're left with what did cause it and it's the cerebral oedema. And then she's looking, I suppose, as you all were, to see what actually caused the cerebral oedema.

A. Well, we looked and we didn't find. Maybe it was ... Cerebral oedema can be the result of very severe seizures, it can be the result of so many things, metabolic disorders, also of course electrolyte disorders. And you're looking into the question of

whether there was an electrolyte disorder in this case --

Q. Yes.

A. -- and that could cause cerebral oedema, but we don't see structural results of that in the brain.

Q. Although I think in your report -- and you can talk us through your short report for the PSNI in a moment -- you were indicating you might see the response to hyponatraemia. That might leave some evidence if you had sought to reduce it very quickly.

A. Yes. Well, there is a particular disorder where usually the result of ... Not always, because I ... Usually the result of iatrogenic interference in the sense that if there's a very rapid change in sodium due to therapy, you can produce necrosis in the brain. But that was not seen in this case and I don't think it occurred in this case. And it can occur through self-medication -- occasionally, I've seen that -- but it also can occur due to rapid therapy to a patient whose sodium is wrong. But nowadays most physicians know about this and it's a rare thing to happen.

Q. Can we go back to the post-mortem cerebrospinal fluid analysis, which is shown in the laboratory result? The white cell count in that -- I think there's 4,000 in a sample containing 300,000 red cells. But in any

event, without me trying to explain the specifics of that, what I would like your guidance on is: is there sufficient in there to warrant a diagnosis of meningoencephalitis from the CSF sample itself?

A. I'm afraid I don't think I want it speak to that. I don't think that is my expertise. I would accept what Professor Cartwright says if he's a expert in that field, but I don't deal with CSF counts, so I don't know. I would have to ask a microbiologist that question.

Q. So if you are looking at just what is within your remit, which is the evidence from the slides, you're just simply not seeing that, any strong evidence -- or in fact any evidence -- that there was meningoencephalitis?

A. Yes. It's very boring, but that's my position.

Q. And then if I just ask you about the hyponatraemia and the inappropriate ADH. I think you've just said in relation to hyponatraemia that that's not really anything, other than a response to something done about it, that you could particularly assist with at post-mortem. If you were conducting the brain-only autopsy in relation to this case and you know, because item 3 is the inappropriate ADH query, and if you'd read the medical notes and records you know that there is some reference to hyponatraemia, is there anything that

you could offer in your clinicopathological correlation to try and assist with that particular problem?

A. Other than what I've just said -- what we have been discussing, ruling out this destructive change that occurs when the sodium is rapidly corrected, no, there isn't. Hyponatraemia per se -- very little is known about how it affects the brain structurally and I don't know that there's anything further I could offer.

Q. The pathologists, in the comment section of the autopsy report, which is where they do attempt -- that is what they claim they're trying to do, carrying out a clinicopathological correlation between their findings and what the clinical problems as identified to them were. They say they can't rule out that the reaction they saw was suggestive of a viral aetiology. That's the slide you were just looking at.

A. Yes.

Q. Although they say:

"With the clinical history of diarrhoea and vomiting, this is a possibility, though a metabolic cause cannot be entirely excluded."

So that history of vomiting and diarrhoea might go to support the suggestion of viral aetiology, of which they've seen a low grade response to or evidence of that, but on the other hand they say you can't rule out

a metabolic cause. Is that something that you would have addressed yourself if you were carrying out the autopsy?

A. You mean in the discussion? Yes. Diarrhoea and vomiting may well change the electrolyte status of the patient if it's severe, but so ... Yes, that might contribute to changes in the electrolyte status of the patient, certainly. If I had been asked about that -- and you say they were -- then I would say, well, that's another possibility. Diarrhoea and vomiting, after all, is a part of many types of disease and it's not necessarily a viral -- you could say it might be part of a viral disease. So, yes, in that sense it raises a flag, but equally, it also raises a flag to the possibility of electrolyte disorder. For that, as you know, you have to go back to the clinical data because a neuropathologist cannot help you here.

Q. Does all that point to, from the way you have looked at it -- obviously there is cerebral oedema, you have seen that. I'm going to come to what you say about it in your report in a minute. You can't really help with the status epilepticus. There's not very much you can do to assist with the inappropriate ADH. You haven't found anything that really indicates viral meningoencephalitis or any meningoencephalitis for that matter. So does it

not all point to the pathologists and clinicians discussing this to say, "Where does that take us now? This is what we saw and recorded in her medical notes and records and this is what we thought was her problem, this is what you say you found". Does that not point to both disciplines trying to see how that is reconciled --

A. Yes. But there may not be an answer. You can't always have an answer. This is the problem. Biology is not physics. So things -- there's a great deal of variety in biology and the results, so we have to bear that in mind. But I agree, it points to having some type of discussion, whether formally or over the phone, with the clinicians as to where this takes us, and they can then ask more, like you, pertinent questions of the pathologist and try and reconcile the data they have. That would be the best thing to do.

Q. An upshot of all of that may be that we may never know with any great degree of confidence exactly what happened and why.

A. That's right. But at least you can ask the questions that people want to -- you know, can you answer them and at least they can posit these questions. Yes, exactly.

Q. And because cerebral oedema is something that was the -- well, everybody recognises she died as a result of it and therefore it was the first of the clinical problems.

I wondered if you could help us a little bit with what you say about the cerebral oedema. It's in your report for the PSNI, 096-027-360. The first thing you say is that there's no evidence of acquired infection. Then you say:

"The cause of death as given on the death certificate and in the inquest verdict is [in your opinion] not concordant with my own observations."

Just to help you, the death certificate had the cause of death as:

"1(a) cerebral oedema, (b) status epilepticus."

Then it had the verdict on inquest was --

THE CHAIRMAN: Sorry, let's do them one by one.

MS ANYADIKE-DANES: Yes. If we stay there and so you see the cerebral oedema, what you're saying in your report is:

"The only relevant observation, albeit macroscopic, is of brain swelling as judged by the excessive brain weight --"

A. Yes.

Q. "-- the effacement of gyri and uncal prominence. However, these are rather weak indicators, not supported by a major downward shift of the brain and cerebellum, which is common in severely swollen brains and by microscopy."

Then you say:

"The lack of vacuolation of white matter ..."

So what are you actually explaining there? Yes, there's a greatly swollen brain, but what?

A. I'm trying to recall the way I was thinking. (Pause). Well, I'm saying that the evidence of cerebral oedema is macroscopic and by weight, but it is not ... Whether cerebral oedema ... That was the whole cause of death, was it, given? There must have been a reason why I said it wasn't concordant. Did I not give a reason?

Q. I think we're looking at it. Do you have it there, Professor Harding?

A. I'm just seeing if I can find it.

Q. If you don't, we can possibly e-mail it to you.

A. I'm not sure whether I can receive e-mails here. I might be able to on my mobile phone. This iPad won't. It's not in that one ... (Pause). I don't think I have that report with me.

THE CHAIRMAN: This is your report for the police.

A. Yes. It must be. I don't think I have that on here.

MS ANYADIKE-DANES: I can read out this because it's very, very short, if you bear with me.

A. Yes.

Q. You say:

"The macroscopic evidence is of brain swelling."

You relate that to the excessive brain weight. In fact, it was 1606 grams as opposed to 1200 grams.

A. I think I recognise my train of thought. Why I wasn't sure whether cerebral oedema was the primary cause of death is because, as I said, it was quite subtle if there was -- by weight, yes, and flattening, I said flattening of the gyri and effacement of the sulci. The base of the brain showed a little bit of uncal grooving, but not tremendous downward displacement, which is what often kills people: herniation of the brain downwards, squashing the brainstem and this produces death. This is, I think, why I was a little bit concerned whether this was the primary cause of death because it was something that was found. I think that was why I was wondering whether that was absolutely correct. I'm not sure what the cause of death was, but that's what I'm saying, that as a primary cause of death there wasn't sufficient evidence. In very young children, you don't see the evidence of herniation because the skull is not fused and there's space for the brain to expand inside the pliable skull. But in a child of 9, if there was severe brain swelling with downward herniation of the brain producing death, you would see the result, and we aren't there. So that's why I was a little bit concerned whether that was the primary cause of death.

Obviously it means I don't know what the cause of death is, but maybe it's unascertained. That's, I think, why I was concerned about that as a definite cause of death.

Q. I understand. So that we're clear, what you're saying is you haven't seen the evidence of it. What was described when the CT scan was done was that there was coning. Dr Squier brought in a consultant radiologist to help interpret the CT scan and I think the upshot of it is he doesn't think it's of huge quality to be able to see some of the things. Dr Squier said it would have been helpful if there had been photographs of that part of the brain so that you could try and see the evidence of the coning that you're talking about or the herniation.

She was understanding your point and I think what she was wondering -- and that we are wondering -- is whether your concern is that you haven't actually seen the evidence of it as opposed to raising a query as to whether you think the brain is sufficiently oedematous to have actually led to coning?

A. Yes. And if I had seen the evidence and it wasn't sufficient, if there wasn't this coning, but the coning was evident in the imaging report, I would have put, "1, herniation of the brain due to", and then I would have

put in brackets "clinical observation due to cerebral oedema". That's really -- I mean, it's a moot point, but that's more precisely what I would have wanted to do as there wasn't obvious -- if there was obvious brain herniation, sometimes it becomes necrotic because it damages the brain just because it's squashed against the skull. If you see that, then you could put that as the number one cause of death, due to cerebral oedema or whatever, or tumour or whatever you find.

But here, I thought it was rather subtle, so to put that just baldly on the top without suggesting that you have clinical cause for this or anything, I thought was not quite concordant with what I saw. I think that was the upshot. It was a precision thing for the cause of death. I felt that, on what I saw, the cause of death was unascertained from the morphological point of view.

Q. Then you say:

"We have no information regarding the other internal organs of the body, which might help us exclude, for example, a cardiac cause of sudden death."

Are you suggesting that in the circumstances it might have been helpful to have had a full post-mortem, or are you simply saying: well, given that I didn't have that information, I can't comment upon whether there

might be other evidence elsewhere in the body to have explained her death?

A. Well, I agree with both those statements. You can't comment because you don't have the exclusion of the general autopsy and I think it would have been useful to have a full autopsy in this rather puzzling situation. It wasn't a cut-and-dried: this is the brain. If the patient had a brain tumour and you knew the patient had a brain tumour and they die of their brain tumour and you want an autopsy, you might consider that it was reasonable to stick to a brain only, but in this case of a child dying relatively suddenly with rather puzzling features, I would have encouraged the clinicians to ask for a full autopsy if I'd been asked. But often, the pathologist is not asked and the clinicians do what they wish to do or the family wishes them to do.

Q. Yes. Then if you were commenting on the cause of death, is it your view, that on the evidence you saw, you can support neither the verdict on inquest nor the death certificate?

A. Well, from what I've said it sounds that that is true, yes.

Q. Thank you. There are some other passages in your police report, but I think in many respects this is the concluding part of your report. You have actually

already dealt with those in terms of the evidence that you saw or, rather, didn't see for the meningoencephalitis, and also the hyponatraemia, which you say is identified from the chemical pathology data. By that, do you mean the lab results of the serum sodium results?

A. Yes.

Q. Your final point is to do with the seizures. And you are again, I suspect, dependent upon the clinical descriptions of what is happening. What you bring to it is that the neuropathological sequelae of seizures were not present, nor was there damage to the hippocampus, which may be seen in children with chronic epilepsy.

A. Yes.

Q. And that remains your --

A. May be seen. Yes, may be seen, yes.

Q. And your conclusion is that although the data are incomplete:

"In my opinion, the evidence suggests that brain swelling was the immediate cause of death and hyponatraemia is the only causative factor that has been positively identified."

And if we're just careful about, or at least, can you explain to us what you mean by that, "the only

causative factor that has been positively identified."

Incidentally, if you have your Blackberry to hand, you may well have received your PSNI report by now.

A. It is here, yes. Whether the pictures will come up ... Oh, "Dr Harding, lines of questioning".

Q. No. What you need is your PSNI report, which is the most recent e-mail that would have been sent to you from us.

A. This is in the last few minutes, is it?

Q. Yes, if it's arrived yet.

A. It doesn't seem to have. Wait a moment.

Q. If not, I can read again what your conclusion is and you can help us with that in that way. (Pause).

A. I've had various e-mails recently, but not one from you yet. The last one was 11 am, which is like half an hour ago, and that's come through.

Q. Not to worry. Let me give you your conclusion again.

A. Well, I heard your question. My understanding was that the only positive evidence of a possible cause of the cerebral oedema was from the chemical pathology results, suggesting there was hyponatraemia. So that's why I came to that conclusion. That was the one positive thing that I -- because I couldn't find evidence of encephalitis, I couldn't find evidence of ... Well, it's not possible to say whether there was ... What led

to the status epilepticus. Status epilepticus on its own can produce cerebral oedema, so perhaps I should backtrack here and say that you can call that another positive thing, but why was there status epilepticus in this case? And since there was no -- I don't know what the ... The only trigger at the moment that's present is the hyponatraemia. So I don't understand, I can't explain everything on the evidence we've got.

Q. If we use your expression, which is positively identified, and if you are taking that from the fact that you have some evidence that she was very hyponatraemic and the evidence is that there are laboratory results that show her well below the normal range at 11.30 the previous evening, she was 121, that's a very low result, and --

A. Yes.

Q. -- that's a concrete thing, a positive piece of evidence in that respect.

A. Exactly, yes.

Q. The reference to status epilepticus, the inquiry engaged a paediatric neurologist, Professor Neville, and he was saying that --

A. I know him very well.

Q. You know Professor Neville?

A. I worked with him for many years at Great Ormond Street,

yes.

Q. His evidence to us was if you wanted to be clear about the status epilepticus then you should have carried out an EEG and that would have allowed you to see what was the electrical activity going on in the brain and you would have been able to be more sure about that. So although you have a piece of evidence that demonstrates the hyponatraemia, in his view, you have no evidence like that that indicates or confirms the status epilepticus.

A. Yes.

Q. And so --

A. I would agree with that.

Q. What I'm trying to tease out is: is that why you highlight the hyponatraemia because in all that you've seen and been shown, it's the one thing that actually has a result attached to it --

A. Yes, exactly.

Q. -- a measured result?

A. Exactly, yes. It's the only measurable thing, yes.

MS ANYADIKE-DANES: Mr Chairman, I think there might be one or two questions from others. I wonder if I could take a couple of minutes to confirm that?

THE CHAIRMAN: Okay. Professor, can you just wait? We're almost finished with your evidence, but

Ms Anyadike-Danes needs to check with the counsel representing the various parties whether they want to ask any further questions.

If you take a break for a few minutes and we'll come back to you, but we'll have you finished in the very near future. Thank you very much.

(4.45 pm)

(A short break)

(4.50 pm)

MS ANYADIKE-DANES: Professor, I have only one question for you, and it may well be a sort of mixed pathology/clinical question, so if I have taken you out of your comfort zone and remit, please let me know.

The question is this: Claire was admitted in the evening of the Monday and she has her terminal collapse in the early hours of the Wednesday, just to give you the scope. When she is admitted, it's recorded by the registrar that:

"[Claire] sat up and stared vacantly, she was ataxic, not responding to her parents' voice and only intermittently responding to deep pain stimulus. She had cogwheel rigidity in her right arm and increased tone in all her other limbs and tendon reflexes were brisker on the right than they were on the left and there was bilateral ankle clonus."

She records non-bilious vomiting since the evening.

Professor Harding, you say in your evidence:

"I consider meningoencephalitis excluded both by microbiology and the post-mortem neuropathology. Hyponatraemia had been identified from the clinical pathological data. There is a history of vomiting, which, when severe, may result in electrolyte disturbance and hyponatraemia is known to cause swelling. The child was said to suffer from seizures. None were witnessed prior to hospital admission [this is all you] ... certainly not status epilepticus ... moreover, the neuropathological sequelae of status were not present, nor was there any damage to the hippocampus, which may be seen in children with chronic epilepsy."

And you go on to say that:

"Although the data is incomplete, in [your] view, the evidence suggests that the brain swelling was the immediate cause of death and hyponatraemia is the only causative factor that has been positively identified."

So this follows on from what we were discussing before and I have just read you out a whole chunk of your report following on from what the registrar had identified.

And the question I'm being asked to suggest to you

is: given that Claire had only been vomiting that evening and had a sodium level that expert clinicians would not associate with clinical symptoms -- there might be a difference of view about that, but anyway this is the question I'm being asked to suggest to you: you had excluded seizures, how would you explain her neurological presentation?

A. I think this is a clinical ... I can't. It's very interesting. She sounds as though she's got some sort of encephalopathy, brain problem, and ...

THE CHAIRMAN: Can you go beyond that, professor?

A. I don't think so, because I think this is a clinical question. The sodium can change very rapidly with very severe vomiting and one doesn't know what level of hydration she had before she had her vomiting. So there are a lot of questions here that I can't answer because it sounds a very clinical question. I'm sorry to be so obstructive.

MS ANYADIKE-DANES: You and, for that matter, Dr Squier gave similar answers to the extent to which the pathologist could be of assistance, and so for that matter did Dr Herron and Dr Mirakhur. Does that all point to something that you said earlier, when I was asking you questions, that this is the sort of case that might benefit from the clinicians and pathologists discussing

matters to see to what extent their combined observations can assist in explaining what happened to the child?

A. Certainly. I mean, both will learn. The pathologist -- we are not in a vacuum, but we need the assistance of the clinician to describe and explain the relevance of the clinical findings in difficult cases like this, and they need us to explain what we found or did not find and whether it will be within the overall parameters that are possible in the case. It's certainly the best practice to do it if you can, yes.

MS ANYADIKE-DANES: Thank you very much indeed for your time.

THE CHAIRMAN: Okay. No more questions? Okay, professor, thank you very much. You've been very, very helpful and generous to us with your time and your contribution. Unless there's anything else you want to add, we're now going to cut the link.

A. No, that's fine. Thank you very much.

THE CHAIRMAN: Thank you, professor. Goodbye.

A. Goodbye.

THE CHAIRMAN: Okay, ladies and gentlemen, that brings to an end today. Tomorrow we're going to have the governance opening by Ms Anyadike-Danes. The written opening was circulated on Monday of last week. We have had some

responses in the last 24 hours, asking us to confirm some factual information. That is being done at the moment and will lead to one or two factual corrections.

I think, Mr McAlinden, some of the responses which came back from your side were comment and there were suggestions that it was a bit unfair and misleading. Those will be dealt with as the evidence progresses, but we'll correct any factual issues which have been flagged up on the Trust's behalf. Those will be adopted in the report, which will be reissued between tonight and tomorrow morning.

MR McALINDEN: I'm obliged, sir.

THE CHAIRMAN: Mr McCrea, we have a provisional opening on your side, which is going to be perfected very quickly.

MR McCREA: I think it is finalised, subject to some minor corrections.

THE CHAIRMAN: There are one or two minor corrections. I think it will be helpful if that can be circulated tonight because, as I understand it, nobody's going to read out the full opening. Ms Anyadike-Danes is going to open orally fairly briefly tomorrow. Mr Quinn and/or yourself will do the same on behalf of Mr and Mrs Roberts and then we have one witness to deal with tomorrow after the openings are complete.

Let's start at 10.30 tomorrow. Okay? Anything else

for today? No? Thank you very much. Tomorrow morning at 10.30.

(5.00 pm)

(The hearing adjourned until 10.30 am the following day)

I N D E X

DR WANEY SQUIER (called) 1
Questions from MS ANYADIKE-DANES 1
PROFESSOR BRIAN HARDING (called) 114
Questions from MS ANYADIKE-DANES 115