Wednesday, 24th March 2021

(10.00 am)

SIR BRIAN LANGSTAFF: Good morning, professor.

THE WITNESS: Good morning, Sir Brian.

SIR BRIAN LANGSTAFF: You can see me?

THE WITNESS: Yes, I can see and hear you.

SIR BRIAN LANGSTAFF: Most of me I hope, and you can hear me?

THE WITNESS: Yes.

SIR BRIAN LANGSTAFF: Now, you are at home, I think, with your wife?

THE WITNESS: Yes.

SIR BRIAN LANGSTAFF: You are on your own at the moment, are you?

THE WITNESS: Now we've set up the system, yes, I am in that room by myself.

SIR BRIAN LANGSTAFF: Let me tell you who you are talking to. Here at Fleetbank House, we have a room big enough number for 200, we have at the moment eight people in it, all of whom, bar one, are wearing masks and that one is Ms Richards, who will be asking you the questions in a moment or two.

Names you will hear are Mary, who will ask you to take the oath in a moment or two, and Soumik, whose job it is to make sure that any documents which we

want to refer you to can be displayed on your screen and to the public generally. The public generally, there were yesterday just under 250 people watching. There will be very similar numbers, I think, today. They are watching from various locations around the country on a mixture of YouTube and live stream. They are the people you are really talking to when you are giving your evidence.

Without more ado, I will ask Mary to ask you to take the oath?

THE WITNESS: I need to get a bible, do I?

SIR BRIAN LANGSTAFF: Yes, you do.

THE WITNESS: Give me a second.

PROFESSOR HOWARD CHRISTOPHER THOMAS (sworn)

Questions by MS RICHARDS

MS RICHARDS: Professor Thomas, can you see and hear me?

A. Yes, I can.

Q. You are Emeritus Professor of Hepatology in the department of medicine at Imperial College London?

A. That's correct.

Q. Prior to that -- I am not going to go through the full details of your career -- from 1974 to 1987 you worked at the Royal Free Hospital teaching, undertaking research and involved in patient care. Is that right?

A. That's correct, yes.

Q. And then in 1987 you took up a post as the departmental chair of medicine at St Mary's Hospital Medical School, and then at some stage after that you became head of hepatology and gastroenterology at the Imperial College Medical School before retiring from that post in 2011. Is that right?

A. That's correct.

Q. Now, you have been a member of multiple working parties, committees and advisory groups detailed in your witness statement. I am not going to ask you to list them, but we will touch on some of them in the course of your evidence.

You gave evidence to the Archer Inquiry and to the Penrose Inquiry. Is that correct?

A. Yes, yes.

Q. And you were then director of the Skipton Fund from around late 2012/early 2013 until 2018 and a trustee of the Caxton Foundation from 2011 to 2018?

A. Yes, that's right.

Q. Now I am going to ask you, first of all, today about the Skipton Fund and the Caxton Foundation and your involvement with both of those bodies, and then I am going to ask you after that some more general questions relating to your work in hepatitis, your involvement in some of the working parties and groups.

A. Perhaps I should say in relation to the Skipton Fund, when it became a company, a limited company, then I was a director -- I think there were three or four of us -- but I wasn't the director, if I could ...

Q. Yes. You were one of a number of directors?

A. Yes.

Q. Our understanding is you were the first medical director.

A. That is right, Ms Richards.

Q. Then you were joined in at that role by Professor Dusheiko two or three years later?

A. Yes.

Q. Now, as I say, I'm going to start with the Skipton Fund, but I am going to ask you about your involvement at a much earlier stage.

So a number of years before you became one of the directors you had some early involvement in the setting up of the scheme.

If we could look at SCGV0000265_004, please, Soumik.

So we can see, professor, this is headed:

"Ex gratia payment scheme for people infected with Hepatitis C as a result of treatment with NHS blood and products.

"Meeting to discuss the medical trigger point

for the proposed higher payment 14th October 2003."

Then we can see who is present: a number of medical commissions, including yourself and Professor Dusheiko, then a number of representatives of the Scottish Executive, the Department of Health and the National Assembly for Wales -- or senior medical officer, I think that must be, National Assembly for Wales.

If we look a little further down, under the heading "Preliminary Discussions", we can see in paragraph 1 it says:

"Following items 1 and 2 on the agenda (Introductions and Background to Scottish Scheme), the experts were asked for their initial thoughts on the medical trigger for the second (higher) payment."

Before we look at some of the discussions in this meeting, can you assist us with this: how was it you came to be involved in this meeting?

A. Well, I had been appointed initially I think in 1987. I was a member of the advisory group on hepatitis. And then I think in 1999 to 2009 I was the chairman. I presume that, since I was already involved with the Department of Health, I was one of the named people who they thought might be able to help. And in particular a lady called Anna Lok, who was an American

research fellow who was working with me, had written a paper describing how one could determine whether somebody had cirrhosis, which is one of the main trigger points for payment of the stage 2 level. They thought that we might be able to throw some light on that particular aspect of the organisation of the -- Skipton, and particularly the transition from stage 1 to stage 2 payments. So I think that's why I got involved.

Q. Now, as we have seen from the heading on the document and paragraph 1, the meeting was specifically looking at the trigger point for the stage 2 payment. Had you been involved in any of the wider discussions about what the shape of the Skipton Fund should be or whether payment should be made on an ex gratia or compensatory basis?

A. No. I was just brought in with the other people that you have got at the heading of this paper as people who could provide medical help -- information, particularly hepatological information on when somebody had cirrhosis, which was going to be one the main trigger points.

That was chosen as a trigger point, by the way, for the larger payments, because up until people have cirrhosis, many are -- or we thought at that stage

many would be asymptomatic. And cirrhosis brought with it all sorts of symptomatic problems and also a change in life expectancy.

Q. Did you, either through your involvement with this group or through your more general involvement with the Department of Health, gain any understanding of why it had been decided that the Skipton Fund would be set up on a national UK-wide basis?

A. No. I really was only involved in this focused issue really of, you know, why this was stage 2 and how could we determine when somebody had cirrhosis without doing a liver biopsy.

Q. If we then look at the terms of paragraph 1, it says in the third line:

"It was felt that this [the medical trigger for the second payment] should be a recognised stage of the disease, rather than subjective symptoms of illness."

Can you assist with why that was the view of the experts?

A. I think it was -- we were looking for objectivity, really, something that would allow whoever to implement this with a solid break-point, really, when you move from stage 1 to stage 2. I think that was the main reason.

Q. And then -- sorry, carry on.

A. Later on actually -- I think you have some evidence -- I was asked to provide a document on, really, the equivalents in terms of symptomology and life expectancies between stage 1 and stage 2 of hepatitis C and HIV, the stages of that, and you have got that in your documents later on.

Q. Yes, yes, and I will also come on to your involvement in what became known as the special category mechanism as well.

A. That's right, yes. I should emphasise, you know, at all stages I was doing research in this area. And as -- as I published papers that showed our initial views may not have been 100% correct -- and this was the case with the SCM, when we realised that some stage 1 patients did have problems of depression, and also a cognitive abnormality which we showed was related to an infection of the brain.

Q. Again, I am going to come on to those. Then we can see the next sentence of paragraph 1:

"All agreed that the trigger point should not be left until too late in the course stage of the disease, as in the late stages patients might have a very poor life expectancy."

Is that the reason why the trigger point was

not limited to liver transplant or cancer, but included cirrhosis?

A. Yes, very much so.

There was one other thing that was included at this sort of earlier stage, before you had a chance of developing liver failure and liver cancer, and that was non-Hodgkin's lymphoma, which was one of the objective determinants of the stage 2 payment.

Q. Now we can see -- sorry?

A. So this is a tumour of the lymphoid system and also requires quite a lot of additional therapies of one sort or another.

Q. Now we can see in paragraph 2 then the discussion alights on cirrhosis as the most practical trigger point. Then there was a discussion about reluctance to make payments contingent upon liver biopsy, particularly for patients with haemophilia, and so a desire to explore the possibility of using non-invasive tests as a viable alternative.

If we then go over the page, so that we can follow through the discussion,at paragraph 5 under the heading "Non-invasive tests" it refers to a range of haematological and biochemical tests, I'm not going to go through each of them but there is a list I think appended to this document, and then halfway through

this paragraph it says this:

"Although these were commonly performed tests, there appeared to be limited experience in using various combinations to predict accurately the presence of cirrhosis in clinical practice. However, there were a number of scientific papers that sought to validate particular combinations of these tests in patients with chronic hepatitis C that could be used as a basis for determining the optimum combination of tests."

Could you just assist us a little further in understanding the difficulty there and the reference to there being limited experience in using various combinations to predict cirrhosis?

A. This wasn't a problem limited to the haemophilia population, but they did have a particular problem because of their failure -- inability of the blood to clot, but it was a common problem with all cirrhotic patients who had coagulation problems and, as hepatologists, we really didn't want to do biopsies until absolutely necessary.

Anna Lok, who, as I say, had been a fellow with me, I think by this time had gone back to the United States to take up an appointment, had written a paper, which was essentially screening describing the APRI

test, which was a computation of an AST, which is a measure of liver cell damage, and a platelet count, which is a measure of how large the spleen is and is a measure of portal hypertension, which is invariably found in patients with cirrhosis.

These two tests together were thought to be the best that was available but, depending on the level at which you set the trigger point and Dr Lok, and subsequently this committee, decided that would be a figure of greater than 2. When the AST started to go up and the platelet count started to go down, then the AST divided by the platelet count would give what's called the APRI score. If you set it at 2, it would be 91% specific. In other words, you didn't pick up people without cirrhosis. The sensitivity, however, at this level was not ideal. It was about, I think, 50% or something like that.

That was the reason why we combined that with the AST over the ALT, because when you have cirrhosis, although both of these tests measure liver cell damage, the AST goes up higher than the ALT when you have cirrhosis. So we combined these two tests, which is now mentioned in the document when people apply for stage 1 or stage 2 payments, and it explains specifically the levels which will indicate that

somebody has cirrhosis. But even so, even with AST and ALT added to this APRI score, there were some people who would have cirrhosis and wouldn't be picked up by these two tests.

So we said that the physicians or nurses looking after the patients could add other data, which might include scanning of one sort, ultrasound, CT and then latterly MRI scanning or endoscopy, when you can look down the patient's throat to see if they have varices, which are an indication that the patient has portal hypertension, which is always or invariably an indication of cirrhosis. You can add in these to make a better platform.

I think over time this was quite a good combination of things. Most of the stage 2 payments were not appealed by the appeal group later on, which is not the case with stage 1, of course.

Q. Yes. Then if we look at paragraph 7 -- paragraph 6 refers to the combination of non-invasive tests and thresholds, as you have just described. Then paragraph 7 says:

"A hepatologist or other clinician familiar with the patient, their circumstances and medical history should be able to advise patients who had not undergone liver biopsy, whether on the basis of the

panel of chosen tests there were grounds for seeking the second payment."

So it would appear that the expectation of this group was that this was going to be a judgment for the hepatologist or other clinician who was actually caring for or familiar with the patient; is that right?

A. Yes, and it had a function in addition to triggering a stage 2 payment and that is related to the fact that patients when they have cirrhosis are at risk of primary liver cell cancer. Between 2 and 4% of people with cirrhosis, irrespective of what it is due to -- so it could be due to hepatitis B or hepatitis C or alcohol or indeed now obesity-related fatty liver -- any patient, particularly males, who develop cirrhosis, because they have this risk of developing primary liver cell cancer, should have yearly ultrasounds to try to pick up the tumours at a time when we could resect them or we could suggest the patient to go forward for liver transplantation.

So we were looking for something that was integrated into the general mechanism of care of patients but would, because it was being done for these routine issues around the patient's care, could also be used to trigger a stage 2 payment.

Q. Then if we look at paragraph 8, it appears that the group within this meeting:

"... recognised that there may be a small number of cases where a panel of simple and readily available tests might not provide a clear answer."

In those cases, is this right, there might need to be further testing. There is relation to the "Fibrotest", is that what we now understand to be the Fibroscan or is that something different?

A. No, it is something different. This was something that the French had come up with, which they were selling via the web as a way of the patients, and indeed the physicians looking after the patients, to tell whether they might have cirrhosis. So you filled in certain bits of information, clinical information, and you then, with a fee, could get the hyaluronic acid or other blood tests done which would say you have such a probability of having cirrhosis.

We didn't like that very much, because what we wanted to do was have something that was -- didn't involve patients going through additional tests. It would use information that was being routinely collected for the care of the patient, as I have already said, so that should they develop cirrhosis, we could start ultrasound screening for primary liver

cell cancer. So we weren't very keen on these additional tests, except the ones that I mentioned earlier, which were also tests being done routinely in British units, you know, such as various scans and endoscopy where there is a fibro endoscope put into the patient's stomach to look. This would be done routinely for patients. That latter test, of course, was a way of seeing whether the patient did have varices. There were ways of preventing the patient having a variceal haemorrhage, which was a catastrophic haemorrhage and very disturbing for the patient. So we wanted to know if a patient was at risk of that so we could give them drugs to reduce that risk.

Lastly -- I have forgotten it. Whenever I used to lecture we were always told don't say you're going to make three points because by the time you got to the third point you couldn't remember what it was. I am sorry, I have forgotten the third point.

Q. It is equally applicable to barristers, professor, so don't worry.

If we go to the top of the next page we can see on the very top line:

"It was also acknowledged that a group of 'experts' might need to be available to adjudicate in

particularly difficult cases."

Was it right to understand that the scheme, as envisaged by this group, was that the vast majority of cases would turn on the opinion of the treating clinician but there might be a small category or small number of particularly difficult cases where a broader range of expert opinion might need to be sought?

A. Basically that's it and, in the period before either myself or Geoff Dusheiko were formally involved, because I had been involved through the advisory group on hepatitis and then this group setting up the issues around stage 2, Nick Fish, who was the administrator for the Trust, would be able to really sign off on a series of patient's stage 2 payments, because these APRI scores and the AST/ALT ratio supported by other clinical information were sufficiently robust that if this information was on the application sheet, this meant the majority would just go through fairly rapidly.

Then, before I became a director, Nick would ask me to help with individual cases if it wasn't -- if the payment couldn't be triggered on the data that was on the sheet, really. But the clinicians looking after the patients would provide the APRI score and AST/ALT ratio and say also which additional test the

patient had done and then say "I think he has cirrhosis or she has cirrhosis, sign off on it", and then this would flow through the system without delays for people like me or Dr Dusheiko getting involved.

Q. If we then look at the heading "Discussion of Item 4 -- Clearance of Hepatitis C Virus", there is then a discussion about whether there should be included within the scheme or not those who spontaneously cleared and those who cleared post-treatment. Can I ask you first of all about those who spontaneously cleared? We have also had them referred to as natural clearers. What's recorded in paragraph 10 is:

"It was agreed that a patient who remained PCR negative six months after the virus had first cleared spontaneously ..."

I am going to leave aside treatment:

"... was highly unlikely to relapse during the course of their lifetime. This was thought to be the case in 98% of cases."

If we just look, before I ask you a question about that, at paragraph 12, we can see:

"Experts agreed that people still had a very small chance of developing liver cancer following ..."

I am leaving aside successful treatment:

"... spontaneous viral clearance."

Now, the scheme that was set up did not include those who had spontaneously or naturally cleared the virus in the way described here. What was the view of the expert group on that issue, as far as you can recall?

A. There were two types of patient who would be identified with antibody and a negative PCR. If I could just remind people that the antibody indicates that there has been infection and would be positive in continuing the infection and also in those who have cleared it, whereas the PCR does detect the continued presence of the virus.

Now, the group -- if somebody has been infected, 20 or 30% of those patients will clear the virus within three to six months. In that group the liver will go back to complete normality. They are not at risk of liver cancer. The group that I think is being alluded to here is a group who, unbeknown to the patient, and sometimes unbeknown to their physicians because they may not have been under a physician's care, they may have moved on to chronic infection and 1% of those is the guesstimate that may then after many, many years clear the virus. They still have antibodies, so they are in the group that's

being talked about here, and if they have already developed cirrhosis, albeit having cleared the virus -- if they have already developed cirrhosis, then they will be at risk of about 1% per year developing liver cancer.

If you still have the virus when you have cirrhosis, then it is about 2-4% develop liver cancer every year. If you have developed cirrhosis but have cleared the virus, either spontaneously, and a few people do that every year, or on these modern treatments which are now virtually 100% effective in clearing the virus, even if you clear the virus but you have developed cirrhosis, you will still be at risk of developing primary liver cell cancer. But it drops to about 50% of the incidence of what you would see if the patient is still having the presence of the virus. Did I manage to explain that okay?

Q. Yes. Can I just ask you, first of all, about the category of those who do naturally or spontaneously clear the virus within a six-month period?

A. Right. Yes.

Q. The decision was taken to exclude that category from the scheme, the Skipton Fund. Was any consideration given either at this meeting or, to your knowledge, at any other meetings to the psychological consequences,

the anxiety, the stress, the fear that that category of patients might nonetheless experience?

A. At this stage I think the answer is no, particularly with at that group who cleared the virus in three to six months.

Later on, when we had been using interferons for a long time, for instance, which, you know, clear only 20% of patients with chronic infection of the virus, this causes quite long-term symptoms. And that was the reason, having observed that -- in other words, once patients had had interferon treatment for treatment of the chronic infection, they would have continuing problems. That was the reason why I thought we should think about having an additional payment in stage 1 patients, and why the SCM came about, and with it, as you will see later, a lot of subjectivity really.

Q. Yes.

A. That introduction later on of an SCM payment in stage 1 was recognition that -- of what you are talking about, but the acute infection, which is people who cleared the virus in the first three to six months, we believed then, and I think we probably believe now, that that group return to complete normality once they have cleared the virus. That

doesn't mean to say they have not had concerns during the three to six months when they have been infected, but after that phase they should, if they have been properly reassured by their physicians and nurses, return to normal or the pre-infection stage, we thought.

Q. Can I then ask you just a little more about what's said here about the position of patients who have cleared the virus following treatment?

If we look at paragraph 13, under the heading "Financial assistance for successfully treated patients", it says:

"There followed a short discussion on whether people who had successfully cleared the virus after treatment should qualify for the initial payment. Experts argued both for and against this."

Then there is a reference to a patient possibly having waited a considerable period before receiving treatment.

Then paragraph 14:

"During this time and the treatment, the patient may claim they had suffered and therefore that they should receive financial assistance. However, this is also the case for a huge number of everyday NHS patients who do not qualify for any assistance.

The danger of treatment becoming a disincentive was also highlighted. Experts recognised that this should ultimately be a policy decision."

Can I ask you to assist with two matters, professor? The first is the reference to the danger of treatment becoming a disincentive. Was it a genuine concern that patients would not go through treatment for what was a very, very serious condition simply because they wanted to obtain financial support?

A. Well, I think at the time I don't think we knew anything about what would motivate people to do one thing or another. But later on, of course, this became a very important issue in so much as, with the current drugs we have, a three-month course of anti-virals clears 100% of patients. And in the last years of the scheme, those of us involved in it often saw patients who had applied for an ex gratia payment after having cleared the virus and -- whereas, you know, they -- at that time we thought they should have returned to complete normality. Unless they had had interferon at the earlier stage, where we know now, and we were becoming aware at the stage that I am talking about, that the interferon could induce auto-immune diseases, it could make rheumatoid

arthritis worse, it could make a thyroid condition worse. It could also make depressive problems worse, to the extent that in my unit we used to refer patients -- or we had a psychiatrist working with us who often gave them anti-depressant treatment before we started interferon treatment because we knew there could be problems during the period of treatment and afterward.

So I think the bottom line is it changed after we had seen what interferon treatment was like, but before then, at the time when we were discussing these issues we, rightly or wrongly, thought that when patients had cleared the virus, then they should return to their pre-treatment, pre-infection stage, and that should be relatively normal, unless there was knowledge that they had problems before, such as anxiety or depressive problems.

So, I mean, this was an attempt at a pragmatic approach I suppose.

Q. Paragraph 14 also says, in the sentence before the one that's highlighted:

"... this is also the case for a huge number of everyday NHS patients who do not qualify for any assistance."

Did the expert group or the group holding this

meeting not recognise that this cohort of patients might be said to be in a very different position from everyday NHS patients, because this cohort of patients had been infected by the NHS, which won't be the case for everyday NHS patients?

A. No. I appreciate that's another factor. We were, you know, not only thinking of the haemophilia patients. We were also trying to provide recommendations for the majority of people with non-A, non-B or hepatitis C. And I should mention here that about 80-90% of people with hepatitis C virus infection had acquired it by mechanisms other than by NHS blood or blood products.

In addition, there was a great deal of complexity around those other than the haemophilia population who had acquired the infection as a result of a blood transfusion, usually for treatment of a malignant state. So I think it was extremely complicated, is what I am trying to say, and we couldn't come up with a group of criteria that were suitable for all situations.

And the ultimate determinant of who got ex gratia payments, of course, was the Department of Health, and then up to the Minister. You will know that the Skipton was, in fact, a body which received money and a set of rules on how to distribute that

money. You might rightly say that I and three or four other people were involved in setting up the rules, at least for stage 2, and that's the case, so we would take responsibility for those rules that were stemming from the stage 2 policy decisions, but the sort of issues that you are talking about became more of an issue in stage 1, where -- not only the issue about, you know, how much people's lives had been disrupted by these infectious agents -- and HIV was added in there as well. There were those issues, but also issues about insurance, all manner of things. So we tried to come up with a set of rules that could be easily interpreted.

Q. Just to complete the picture about these early discussions, there's a second meeting to discuss the medical trigger point in January 2004.

Soumik, that's at DHSC0004425_159.

We can see there it is the second meeting, 27 January, and the attendance there set out, including yourself.

I am not going to go through the detail of it, but if we go over the page and we just look at paragraph 4, you have referred already to Dr Lok. Is that what is being referred to here, the work that had been undertaken by Anna Lok?

A. That's right. And the two tests that ultimately were on the application form for stage 2 payments were the APRI score and ALT/AST ration. And it explains there what the trigger points are, what -- the APRI score should be greater than 2 and the AST/ALT ratio should be less than 1, if cirrhosis is present.

And that really had been tested by Dr Lok in a prospective way; in other words, once she had decided this might be satisfactory, then she looked at it in a group of patients who were going forward for liver biopsies. She would then, for other reasons, determine what sort of liver disease they had, as opposed to the severity. She would look at these tests and see how they correlated with the liver biopsy, which was the gold standard, if you like, for cirrhosis.

So yes, it was that -- APRI score and the AST ratio is what was taken forward into the forms, and the physician or the nurse filling in the form with the patient would mention these. And if they were positive and they had already been receiving a stage 1 payment, indicating that it was accepted that they had been infected from NHS blood or blood products, then that -- Nick Fish, I think, would automatically pass those through to -- for payment,

without consulting the medical people.

Q. If we go to the next page, 15, we can see that process I think that you described clearly envisaged there. Paragraph 15, under the heading "Whose responsibility?":

"In the first instance, it was suggested that the patient/patient's clinician should initiate a claim. If not by biopsy, this would require submitting the application form, presenting the clinical information from the test(s) to the Skipton Fund. If the results were clear-cut ..."

Then we see the criteria there set:

"... the claim would be validated and authorised by the fund. If not, a medical panel would consider the results or perhaps commission Poynard 'Fibrotest'. If still inconclusive, it is envisaged the medical panel would review the case."

So that, I think, is what you were describing: the group's understanding of how the system was going to work?

A. Exactly.

Q. If we just look at the very bottom of this page, under the hearing "[Any Other Business]", in paragraph 19:

"Following the tabling of the press statement that announced the details of the Skipton Fund,

Dr Giangrande and Professor Bassendine both expressed disappointment that the scheme had not been extended to dependants of those who had died."

Had you been involved in any discussions about whether the scheme should or shouldn't include dependants?

A. Well, somewhere along the line, and I can't remember whether it was the Archer or the Penrose that I had also been involved with, it did seem that this was an important issue, that -- and particularly in the haemophilia population, where, because it is -- can occur sporadically, but is often genetically determined and affects males, is -- and often, except in today's world it is probably no longer true, the men might be the person supporting the family, it was -- you know, if that person died, then it would leave the family in a terrible situation.

So I think we also shared the concerns that Maggie Bassendine -- I don't know Dr Giangrande, but I do know Maggie Bassendine, who worked for me for a long time. I shared her views. I think it had been mentioned in the Penrose, had it not?

Q. Yes. That was rather later.

A. Right. Yes. It is difficult, when I was involved in all those things -- those two or three things, to

remember what was decided at what situation. But I think there was general agreement with what Maggie Bassendine said there.

Q. Now, I am not going to go to the document, but following this meeting, I think, you were copied into some e-mails, as were the others of the group, that looked at the design of the form. Did you after that -- so that was in early 2004.

We know the Skipton Fund became operational in July 2004. Did you after that have any ongoing involvement with the Skipton Fund other than such approaches as Nick Fish might make to you about individual cases prior to your appointment as a director?

A. I can't remember the temporal sequence. I was trying to do that this morning and trying to find out what Nick had said actually. Because I thought I had been involved before 2011, which is the point when I -- I think it was 2012 I was actually appointed to be a medical director, but I've got a feeling I was involved in individual cases before then, but certainly my formal arrangement came after I was appointed to the Caxton, which I think was 2011.

Q. Yes.

A. And it soon became apparent that I didn't have a big

contribution to make there, because I wasn't more -- the Department of Work and Pensions and these sort of things, and I gave a talk to the Caxton at the beginning on some aspects of the history of -- and the main problems in hepatitis C. And then I was invited to become a director of the Skipton in a formal sense, but -- I cannot remember where the break-point is but I am pretty sure I was involved before that actually. But Nick Fish ought to be able to tell you that, so -- so when I came -- but the formal appointment was in 2011.

Q. Again, I am not proposing to take you to individual documentation relating to this, but I think it is also right that you provided witness statements for the Department of Health in response to two separate judicial review challenges to aspects of the Skipton Fund, one I think in around 2010, when there was a challenge about the position of those who had cleared the virus, and you provided a statement, and then I think later in 2017 you provided a witness statement for the Department of Health in a challenge that looked at the comparison between HIV and hepatitis C. Is that correct?

A. Yes. I certainly remember the second one, trying to compare hepatitis C with HIV, yes. I can't remember

too much about the earlier one, to be honest. I'd need to see those documents again.

Q. I was not proposing to ask you any questions about --

A. It's okay.

Q. -- professor, but it may explain why you had some recollection of some other involvement.

I just then want to turn to 2012. And this is shortly before you, I think, became a director.

If we go to SKIP -- just let me get the reference -- SKIP0000030_011, please, Soumik.

These are the minutes of a meeting of the board of directors of Skipton, 26th March 2012. If we go a little further down the page under the heading "Matters Arising", it says:

"The Scheme Administrator ..."

So that's Mr Fish.

"... reported that the expected increase in borderline stage two applications had occurred. As a result, a meeting had recently taken place with Professor Howard Thomas, a world expert in hepatitis C and liver disease, during which a collection of borderline claims had been discussed. The meeting had been extremely useful and resulted in a decision being made on each case to either approve, decline or write back to the applicant for specific further

information. The meeting had been useful in pinpointing biochemical trends which are indicative of cirrhosis as well as other symptoms which are significant when assessing the likelihood of advanced liver disease. When borderline claims are received in the future, the lessons learned from Professor Thomas would be applied, with the option of referral to him if there is any doubt."

There is then a discussion about Fibroscan, or transient elastography, and we can see one of the directors, Mr Spellman:

"... asked if there was a recognised 'trigger' at which a Fibroscan reading was indicative of cirrhosis. The Scheme Administrator responded that a reading of 15 was accepted as being 90% indicative of cirrhosis based on information provided by Dr David Mutimer, a leading liver specialist who is also a member of the independent appeal panel. The Board requested that this reading be double checked with Professor Thomas."

Now, I am going to come on to the Fibroscan trigger in a moment, so if we could just leave that aside for a moment. Can you recall anything about the broader discussions as it how to deal with borderline claims that you and Mr Fish appear to have had and, in

particular, what's said to be biochemical trends indicative of cirrhosis and other symptoms?

A. Yes. I mean, other than the APRI score and the AST/ALT ratio, I mentioned earlier if someone has cirrhosis then blood has difficulty flowing through the liver, which makes the spleen become larger, then the spleen takes out of the circulating blood platelets. So when somebody has cirrhosis, the blood can't go through the liver so readily and all the blood from the intestine, I should say, and from the spleen goes up through the liver.

But if that flow is impeded, the spleen gets larger, the platelets go down, and either a low platelet count or endoscopic evidence of -- endoscopy is where you have a fiberoptic scope popped down into stomach, where you can seek the lining of the stomach -- if there is portal hypertension, difficulty in the blood going through the liver, then the veins in the lower oesophagus and stomach are distended. So that is evidence of portal hypertension and invariably indicates cirrhosis.

So that would be one set of observations that would also lead to cirrhosis.

The Fibroscan was a mechanism whereby you put a sheering impulse into the liver through

transaminases, that's the ALT and the AST, which normally should be within the liver and when the liver cells are damaged leak out, so the blood levels are higher, those tests only tell you about whether there's ongoing liver damage. But the liver also makes coagulation factors, albumin, and a whole host of the other proteins. All the proteins in the blood are made in the liver. So when the liver shrinks in size, which happens with cirrhosis, then the albumin particularly goes down. The coagulation factors also become abnormal, not helpful -- still helpful in the haemophilia situation, because there are ones which aren't abnormal in haemophilia, but are reduced when the liver size is reduced by cirrhosis.

So those three main groups of things -- portal hypertension evidenced by endoscopy, stiffness of the liver as measured latterly by the Fibroscan, and the inability of liver to produce the blood proteins because of a reduced liver size -- would be other bits of information that might make us think and, in particular, the physician or the nurse helping the patient fill in the form might put in there to convince Skipton that this was a case of cirrhosis and should trigger a stage 2 payment.

Q. If we look at a meeting the following March, we can

an ultrasound probe and you look at how much the liver wobbles, much as a jelly, you know, would wobble if you shook it. A normal liver would wobble quite a lot, whereas one which has cirrhosis would become stiff and wouldn't wobble. That was the basis for the Fibroscan.

I think later on, and you may be coming to this later on, I think we thought that we should have a lower score than 15. I think was it 12 or something like that?

Q. I am going to pick that up with the next document we look at, Professor Thomas?

A. Yes, because I thought that 15 -- David Mutimer's thinking, really, was that he wanted to get specificity up high; in other words, he didn't want to misdiagnose cirrhosis, but that would mean when you increased the specificity, then the sensitivity goes down. So I thought we would be better and fairer to the patients if we set it at a lower level where we would let some people through who didn't have cirrhosis but were probably very near it anyway and we wouldn't miss many. So that's the component of the other tests.

The other things that happen when you are near to cirrhosis is that the liver, as well as releasing

see the issue of the Fibroscan being picked up. That's SKIP0000030_085, please, Soumik. We can see this is 11th March 2013 meeting of Board of Directors of the Skipton Fund. You are present and we can see from the first paragraph:

"Welcome to Professor Thomas.

"The Board welcomed Professor H Thomas a director and looked forward to his expert help."

So this the first meeting, as far as we can understand it, that you attended as a director. Then if we look towards the bottom of the page, we can see the issue of Fibroscan being referred to:

"The Scheme Administrator referred to the Fibroscan reading that was considered to be indicative of cirrhosis."

Then there is reference to Dr Mutimer's view which we looked at in the previous set of minutes. Then reference to a medical bulletin having been submitted, taken from the Hong Kong medical diary which suggested a reading of 12.5 or over as an indicator of cirrhosis. Then this records you citing:

"... a NICE study into the effects on the liver of hepatitis B which suggested that 10 ... or above was an indicator that cirrhosis might be present. It

was agreed that, due to the range of differing opinions, all transient elastography readings (of which Fibroscan is one brand) would continue to be considered along with other test results and markers to determine the likelihood of cirrhosis. Borderline applications would be referred to Professor Thomas for his expert opinion."

So that appears to be the way in which the issue of Fibroscan reading was addressed at that stage. No absolute cut-off point one way or another, but not reliance upon -- or not requiring a reading of 15 or above; is that right?

A. Yes, and I rapidly thought when that responsibility decided on me, who else I could get to be involved, and that's where I thought it would be a good idea to get Professor Dusheiko involved, because I think when there are -- you know, when it is marginal, it is good to get other people's views and that's why I got -- put forward -- got Professor Dusheiko involved as well, because he was equally well-informed in this area as I had become.

Q. Then there is one further discussion about Fibroscan readings I want to ask you about. It's a couple of years later, SKIP0000030_068. So we can see these are the minutes of the meeting of the Board of Directors

of Skipton, 10 March 2015. You are present, as is now Professor Dusheiko. We can see from the "Welcome to the new Director and Finance Manager" that this is Professor Dusheiko's arrival on the Board of Directors. If we then go to the bottom half of the page, there is reference under the heading "Matters arising". If we just look at the paragraph that has the number 165 next to it, it says:

"The Scheme Administrator reported that, since the Fund had greater board level medical expertise, the success rate at the more recent Appeals Panel meetings had been less than the overall average of circa 50%. It was agreed that the appointment of Professor Dusheiko meant it was no longer deemed necessary to appoint another medical director, especially as there was often good medical data published online to assist with applications where records of a medical procedure were provided but not specifically that referenced treatment with blood or blood products."

Now, that's obviously concerned with the stage 1 process, but was it your understanding that fewer cases were being overturned on appeal because of your and then Professor Dusheiko's involvement with the stage 1 process?

A. Yes, in short, but I thought we had a bigger effect on -- well, I mean, there was already very few cases of stage 2 refusal overturned by the Appeals Panel, I thought, and that was because that was highly objective in the way that we have just been discussing. It was the stage 1s that were the problem really, where it had to be more than 50% probable that the individual had received NHS blood or blood products at a time when medical records were often not available.

We went to extreme ends to try to provide, even before the Appeal Panel were involved, evidence to suggest that they had received a blood transfusion. But that was a soft process made a lot worse by the fact that I think after seven years most records were no longer available, in general, not just in this setting. So, for instance, if you had been involved in a road accident and your pelvis had been fractured or one of the long bones of the leg had been fractured, it was likely you would be having more than two units of blood.

So I went online and asked the question of how many patients, you know, who had been involved in a road accident and had fractured their pelvis would receive a blood transfusion, and there's a NICE study

on that showing that virtually everybody did. So we were able to say anybody with scars showing they had had a fracture of the femur or historical evidence that they had had a fractured pelvis, then we could say that would be taken as evidence.

So we are trying to build a case to help those that had -- who were putting in a stage 1 application at a time when they couldn't actually lay hands on notes really, and Geoff and I -- Geoff Dusheiko and I -- often met to think of ways in which we could do that, for instance, taking photographs to see what sort of operation they had had. It might seem strange but patients actually went along with that and sent a picture to show they had had a caesarean section, where quite a few patients would have a blood transfusion and these sort of issues really.

Q. I will come back to stage 1. If we go over the page whilst we're on this document we can then pick up --

A. Stage 2 then, specifically, we did manage to get that down to a very good level of acceptability and with very few appeals overturning.

Q. We can see the discussion in the long top paragraph on this page, further discussion about Fibroscan readings. So it says:

"Professor Thomas reported that he had recently

attended a British Association for the Study of the Liver/British Society of Gastroenterology meeting about the new HCV treatments during which he summarised the Skipton Fund's assessment process for determining if cirrhosis was probable for the stage 2 payment. The data supported a Fibroscan score of 14.5 kPa as an indicator of a greater than 50% probability of cirrhosis in the absence of other markers. At the meeting the clinicians had recommended a Fibroscan score for advanced fibrosis ... of 11.5 ... which was lower than that used for Skipton Fund stage 2 assessments, as they wanted to make sure the sensitivity for offering treatment was high ([over] 80%). Although a good approach from a treatment point of view, as it limited the chance of missing a patient with cirrhosis, from the Fund's point of view it would mean that cirrhosis would be overestimated in many cases. Professor Thomas would make the Department of Health aware of this difference in approach and that, unless requested otherwise, the Fund would continue to consider applications for evidence of a greater than 50% probability of cirrhosis."

If we just go back up the page so we see the whole of that first paragraph, Soumik. Thanks.

course, when it got to 6 and they had cirrhosis then they would be at risk of developing primary liver cell cancer.

So I felt uncomfortable watching this and this was at the stage when these new drugs came in, which were virtually 100% effective. So I thought we should be giving these new drugs to people in the pre-cirrhotic stage, Ishak 5, rather than waiting until they had cirrhosis. The Department of Health had already decided that patients with cirrhosis would get these drugs before it had been considered by NICE, and I think they made provision for 500 people to get this, but I wanted to include, for the reasons I have just said, that Ishak 5 should be included, and that didn't come about, because -- I don't know why, it wasn't my decision. But I wrote to the Minister saying I thought we should do this and it didn't come about.

But that's why, because that was going on in the background, I thought we should be moving down to a Fibroscan score of about 12, really because we would then be including quite a few of these Ishak 5s. If you like, it was a covert way of getting these patients into the scheme.

Q. This document reads as though the score that was as

This would tend to suggest by this stage, March 2015, the Skipton Fund was using 14.5 Fibroscan score as its indicator of a probability of cirrhosis, whereas what we looked at previously suggested it was going to be lower than that. Can you assist us with understanding the position?

A. I mean, we did move it downwards. There is no doubt about that and we alighted on 12. That was principally because Ishak 5, which is just pre-cirrhotic and Ishak 6, which is cirrhosis, are not that different, even at a biopsy level. I was concerned that -- I think I included -- at one stage when we were doing serial Fibroscans, it was apparent that some patients were moving from a pre-cirrhotic to a cirrhotic stage.

Pre-cirrhosis would be 5 to cirrhosis at 6. Once you have cirrhosis, as I mentioned earlier, then, even if the virus is cleared, you don't go back to lower levels of fibrosis and ultimately to normal, whereas if you are treated at Ishak 5 and you get rid the virus, the liver goes back to complete normality. We were seeing patients who were having serial scans who were moving from 4 or 5 up to 6, you know. During the period of a year there were 90 cases I brought to the attention of the Department of Health. Then, of

a matter of fact being used by the Skipton Fund was 14.5. Is it your recollection that that's not correct then?

A. I can't really remember, to be honest. I remember the meeting with the British Society of Gastroenterology, where we did come on to, you know, this figure of 14.5, but I think it is recorded somewhere we did decide to use the figure of 12 in the Skipton. So, for the reasons I have just said, I thought it was better to include those slightly lower levels, because we might pick up some that were going to process to 6 in the very short-term, namely the next year.

SIR BRIAN LANGSTAFF: It might depend upon the quality of the person who took the minutes or the quality of the minutes rather, because the reference to "the data supported a Fibroscan score" might not be the conclusion of Professor Thomas, it might be his report of what the British Association made of the data, in context.

MS RICHARDS: Yes, indeed. It is not clear.

SIR BRIAN LANGSTAFF: It is not entirely clear.

MS RICHARDS: Which is the reason for asking the question, sir --

SIR BRIAN LANGSTAFF: Obviously.

MS RICHARDS: -- because the documentation doesn't, I

think, provide a clear answer.

Professor, do you know whether the Skipton Fund published anything about what its approach to Fibroscan scores was so that clinicians would know whether it was worth assisting their patients to make an application to the Skipton Fund on the basis of a Fibroscan result or not?

A. I can't recall whether we did or didn't, really. Certainly, the British association for the study of the liver, BSG, did -- that was published. I mean, the BSG and EASL, and the British Association, always published their meetings, because the British Society of Gastroenterology owned Gut and they tended to put these sort of policy decisions into Gut so everybody could see it. But it was a contentious issue really, not just from the point of view of whether patients should get an ex gratia payment but, as I mentioned before, when patients were deemed to have cirrhosis, they are at risk, 2 to 4% per year, of developing primary liver cell cancer, and that requires that they have some form of imaging, usually an ultrasound but possibly a CT scan or MR scan, so that the tumour is picked up when we could resect it or recommend the patient for a liver transplant.

So that meeting of the BSG was also serving

that function. It wasn't purely on the issue of whether the Skipton stage 2 payments would be triggered. Professor Mutimer, of course -- actually, he was on the Appeal Panel at that stage, was he not?

Q. Yes.

A. I think he was very keen to be as precise as possible, really, and I was a little bit more on the side of sort of saying "It is going to be in the patient's benefit to go for a slightly lower level", which is why I thought we agreed on 12 in the end.

What is agreed at this meeting is one thing, about what Skipton decided to do, which I am surprised can't be found -- I would hope it could be found somewhere in the minutes of various Skipton meetings, I am pretty sure we agreed with 12.

Professor Dusheiko might be able to help there --

Q. Thank you. We will check that.

A. -- because he might recall better than I can, probably.

Q. I want to go back then, on a different issue, to the previous set of minutes we looked at, so that's SKIP0000030_085.

So this is the March 2013 meeting, your first meeting as director again.

If we look now at the second page --

A. It is important to say "a director", by the way, because we had group responsibility. I think you are promoting me to a level that I didn't attain. Peter Stevens was "the director" -- the chairman of the directors I should say.

Q. If we look at the bottom of the page, we can see that the board considered here the issue of "Stage 2 applications from the estates of people who were co-infected with hepatitis and HIV, who died before 29th August 2003 and whose records have been destroyed".

Then we see:

"The Scheme Administrator reported that there had been a number of Stage 2 applications from the estates of people who had died and whose records had now been destroyed. In many cases it was apparent that the family member, most often a widow, distinctly recalled that the deceased had been diagnosed with cirrhosis, but because of the lack of records the application had been declined. Some of these cases were also declined by the Appeal Panel, which had then undertaken extensive research into the matter."

Then there is a reference to a suggestion by Dr Mutimer. Then it is the next paragraph I wanted to ask you about. It says:

"After further meetings and research, and with the help of Professor Thomas, a model had been created based on average fibrosis progression rates in people who were mono-infected with hepatitis C and co-infected with hepatitis C and HIV. The Scheme Administrator summarised the model, the values and dates that had been used ... and the reasons why these figures had been used. Around 40 declined applications from the estates of co-infected people would need reviewing on the basis of this model."

Can you assist us, because I don't think we have the underlying model itself, with what this model was and what it told you and how it was used?

A. I can't remember a heck of a lot about this, I am afraid. There was a paper produced, and I think Professor Dusheiko was involved with this, plus one of the Cambridge mathematical modelers, and the focus was to look at people with hepatitis C mono-infection as opposed to those with hepatitis C and HIV. That allowed us to come up with a formula really for saying that -- depending whether they had the mono-infection or the co-infection, what would be the probability in the absence of a post mortem that that patient had cirrhosis.

I could look up the papers again, but that was

essentially the summary. I can't remember, you know, what the detail of the formula was, but -- and that did mean that we could say with a reasonable probability, the magical greater than 50% probability, that the patient had cirrhosis and had died, and -- and no post mortem being done, of course, which, in the case of HIV co-infected individuals, there was a reluctance to do this, so it was required that we should have some sort of model.

I can't really say anything more about the detail of it, but I could look it up in due course if you wanted.

Q. Thank you. I think we understand from other documents it is described as giving rise to predictive formulae for progression to cirrhosis?

A. Yes.

Q. So the aim was to apply it, whatever precisely it looked like, to the cases of those who were dead and for whom no records, or no relevant records, existed to work out what the possibility was that they would have progressed to cirrhosis by the time they died. Is that right?

A. Yes -- I am sorry. A bird is just banging on the window, so I was distracted there.

Would you mind saying that again?

Q. Yes. It was, as we understand it, a predictive formula -- that's how it is described in other Skipton documents -- for progression to cirrhosis?

A. Yes.

Q. So whatever the precise data was -- it perhaps does not matter for present purposes -- it was then applied to work out what the probability was that someone who was dead, for whom there are no records or relevant tests, would have progressed to cirrhosis?

A. Correct.

Q. Sir, I note the time. I am going to move on to stage 1 applications in a little more detail now. So perhaps this is a good moment for a break?

SIR BRIAN LANGSTAFF: Yes. We will take a break until 11.45. It will allow you to get some refreshment, professor, and those who want to do the same. So 11.45.

MS RICHARDS: Sir, I can't remember whether you gave the professor the warning.

SIR BRIAN LANGSTAFF: I haven't.

Let me just tell you what the rules are. You must not during this break, or any other break that we may have, discuss with anyone the evidence you have given or the evidence that you are yet potentially to give. You can discuss that after you have finished

your evidence, but not before. But in the meantime you can just talk about anything else you like.

11.45.

A. Okay.

(11.18 am)

(Short break)

(11.45 am)

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: Professor Thomas, I am going to ask you a little more about the stage 1 decision-making process now. I am going to ask you to look at a passage in your witness statement.

Soumik, could we have WITN3824007, please, and if we could go to page 29.

That's different from the version I have got. Give me a second. Okay. We can pick it up at the top of the page. So this is in paragraph 112, I think, of your statement. It says:

"In general patients were concerned about the evidence needed to establish that the PTH [post-transfusion hepatitis] was probably (greater than 50% likely) due to NHS blood and not other means of infection such as IVDU, tattooing etc. All haemophilia patients who had received factor VIII concentrate were automatically accepted as infected by

NHS material; this was established by several prospective studies showing that the incidence of abnormal ALTs after concentrate infusion, both in the literature and our own study, was almost 100%. Nick Fish signed off on these cases without clinical input."

Then you turn to transfusion cases and say this:

"In cases of blood and plasma transfusion, we had to say that it was more than 50% likely to be due to transfusion. In the absence of GP or hospital case notes this was very difficult. Occasionally we had evidence of a major operation where in virtually all cases blood transfusion would have been necessary eg cardiac valve replacement or major trauma resulting in pelvic or femur fractures. These cases usually involved both Professor Dusheiko and myself and involved detailed consideration. In my view this was as objective as possible.

"In the absence of case notes it was almost impossible for Professor Dusheiko and myself to provide this level of certainty. In many cases all we could do was to exclude non-transfusion related modes of transmission such as body piercing and IVDU. Sometimes we had evidence of surgery which did not

usually require transfusion but infrequently did; this again required clinical judgement."

Now can I ask you, first of all, just to assist us with understanding how you would use your clinical judgement to make the assessment of whether the applicant was probably infected by blood transfusion?

A. Well, it's really just a second way of saying what I have mentioned earlier, in so much as if, you know, a surgical procedure or, as I mentioned, trauma were invariably needing transfusion, then that was -- then we would take that as given. And the way we established those precedents, if you like, was by going to the literature.

So I would Google in, as I think Professor Dusheiko did as well, you know, "percentage of patients receiving blood during aortic valve replacement" or "during the pinning of a pelvic fracture". Surgeons have often, and indeed haematologists, have looked at series where they can provide this sort of data. Where we find that, then we sort of moved that on to the group of patients needing just a sign-off without any further consideration.

I mean, there was very little else that one could look at. There were GP's notes, which in the

main were not destroyed after seven years, which seems to be the case in hospital-based medical practice. Many GPs have these sort of cards where they, you know, note down over maybe 20 or 30 years what has happened to a patient. So, you know, occasionally we would find in a woman that she had had, you know, a major haemorrhage during delivery of a child. So, you know, we know that caesarean sections, you know, with placenta previa, often results in massive haemorrhage. So there were little incidents like that where we did our best to say, "Well, in most cases this would require transfusion". That's what I meant by "clinical judgment". Whereas, in contrast to stage 2, it was -- as I say, it was cast iron dependent on the APRI score and AST/ALT ratio.

Q. What about cases where there were no medical records revealing a transfusion, either because the records had been lost or destroyed or because they are incomplete or, as may often be the case, they don't actually record the administration of blood, and you can't say, as a result of your research, "These are cases which almost invariably involve a requirement for transfusion", but you do know, either on the basis of what the applicant has told you or on the basis of what their GP has told you, that they had some form of

surgery? How would you approach those types of cases? Would those applications be rejected if you couldn't find anything in the notes that gave a hint of a haemorrhage?

A. Yes. In the main that would be the case, because I took the view, when I was doing this by myself, that if at that stage there was no evidence -- it was our mandate to say whether it was more than 50% likely that the transfusion had occurred. If there were no notes and no evidence of the type that I have been describing, then I couldn't say that. But I know that Nick Fish and I also would point out that the patient could appeal this. And the appeal group had a much stronger position. You know, their view would be held, irrespective of how solid it was -- when I say "solid", medically based.

Indeed, for some time there was a minimum of medical input on the appeals group. I think only one of the people were medically qualified. So I took the view that -- you know, large sums of money were involved, the Department of Health were taking this out of the NHS budget, that I should, you know, use my medical knowledge to take out those cases where I could definitely say there had been NHS blood or blood transfusion and no evidence of other

possibilities. For instance, you know, some people -- there was one case where the gentleman was taking methadone, which is usually only given for intravenous drug use, and he argued that he had only taken non-intravenously administered drugs. So, I mean, one could weed out cases like that and go through, in a positive sense, the ones where there was evidence of blood transfusion, and then it was up to the appeals group to use a much more subjective set of rules. And their opinion was final. So I thought that that fallback position safeguarded the patient's interests should, on further inquiry, something else came up that I or Geoff hadn't noted.

Q. We know both from the documents and from Mr Fish's evidence that at the stage of Mr Fish looking at it with the assistance of one of the directors, what was looked at was essentially medical information, what the record showed or didn't show. There was no provision, for example, to consider and receive a personal statement from the applicant setting out their recollection of events or a statement from a family member setting out their recollection that their relative had received a transfusion, whereas that material could be considered at the Appeal Panel stage.

A. Yes.
Q. Was there any reason you were aware of as to why that information couldn't be considered at the first stage by the administrator and a director?
A. We did see cases where what you said was the case, and a relative would say, for instance, "Well, when I came in to see my husband", or wife or what have you, "they had an intravenous transfusion device up, and I could see", the relative would say "and I could see a little bit of blood just near to the point of insertion through the skin". And always, in any transfusion of clear fluids, in other words, saline for rehydration, there is always reflex of blood into that last 1 to 2 centimetres of the tubing, and that, for someone who isn't involved in medicine or transfusion, they would take to indicate cast iron visual evidence of transfusion, but it isn't.

So we listened to everything, and Mr Fish actually often had conversations with the person on the telephone to recommend evidence that might be provided, but -- I make no bones about it, this was an extremely difficult stage of the assessment and why I initially, and latterly Geoff Dusheiko, put so much emphasis on objective evidence that we could bring forward for stage 2 payments, because we were quite

aware of the fact that the stage 1 process was, you know, highly subjective.
Q. Your statement refers, in the bottom paragraph on the screen, to how:

"In many cases, all we could do was to exclude non-transfusion related modes of transmission such as body piercing and IVDU."

Did it ever occur to you or any of the other directors or Mr Fish to take a slightly different approach to stage 1 applications and look to see which was the least unlikely mode of transmission?
A. The least unlikely.
Q. If I can suggest a hypothetical scenario to you. You had someone for whom no evidence whatsoever to suggest they had ever had a tattoo or a piercing or any likelihood of sexual transmission, which we know was, I think, a low risk in any event, and no evidence whatsoever to suggest intravenous drug use, no evidence of overseas medical treatment of a serious nature. They had to have got their hepatitis C somehow. If they could point to some form of surgical intervention that they had undertaken within the NHS, why not take the approach of looking at which is the least unlikely: that this 70-year old individual, married for 50 years, has been infected with HIV

through a drug or sexual route or they'd been infected via transfused blood?
A. Well, I think that, in retrospect, could have been a way of proceeding, but I took the view that this attitude could be applied at the stage of the appeal. We did recommend in the letter that Nick sent out that the appeal process was open, and a very large number of the people where we had not found positive evidence for involvement of NHS blood and where these other risk factors were not present, a high percentage of these did go on to appeal. So we felt that this was the stage at which that could and should happen.

We, at every corner really, tried to do the best by the patients, and make sure there was some uniformity of the process that was being used. We didn't talk to the Appeal Panel in these terms, but I think every single letter would say, you know, "We can't find any involvement of NHS blood here, but it is open to you to go to the Appeal Panel". So we felt we had not been inappropriately -- you know, we had not been putting the patients to a major disadvantage really.

And many of the comments or the evidence the patient came up with were of the type that were completely plausible. I mean, this business of,

"Well, I could see that there was a transfusion in place and there was blood staining in the area, the last 2 to 3 centimetres, does this not indicate the patient had a blood transfusion?" The answer is no, but it is quite reasonable the patient would believe this is the case and the patient's relative would also believe this was the case.

As I say, we were of the view this would then be -- the Appeal Panel could actually say, you know, "Well, we think, on balance, there is no reason for not believing this patient. Let's pass it through".
Q. Now, you and Professor Dusheiko -- sorry.
A. Do you think that was unfair? I mean, there was a well-trodden track for the patient to continue to prosecute their claim in the system, if you like, through the appeal process.
Q. You and Professor Dusheiko, your area of expertise, both of you, was hepatology?
A. And general medicine. We both did general medical take, we call it, where for one day a week, usually, you take all the cases that come into an acute hospital. Then you look after them for 24 hours, the next day you usually get a specialist to look after them, unless it is a more pressing concern, where you get a cardiologist or an endocrinologist to help

during the night hours.

Q. You would be having to make clinical judgments about whether a particular operation or intervention might have required a transfusion. Was there ever a system in place or contemplated whereby other medical experts -- perhaps an orthopaedic surgeon if it had been orthopaedic surgery, or an ENT specialist if it had been ENT interventions -- to ask for their take or input? Was that ever considered?

A. Yes, and that's why we went -- we didn't actually -- the way of getting that bit of information, of course, was to look online at the literature, look at NIH PubMed, which is a way of accessing all medical literature. You could just ask, you know, "percentage of patients undergoing an operation who received blood?" and it is surprising how much of that type of information is in there.

For instance, tonsillectomies very rarely, if ever, require a blood transfusion, whereas pelvic fractures and fractures of the femur do, you know. So that information is there without having to ask one particular surgeon. These were series that you could find through NIH PubMed. NIH is National Institute of Health and PubMed is a public database. You could actually find the date when it was done, because blood

requirement for an operation varied over time. So you could look then at when the paper was found in NIH PubMed database, it would say "published by so and so surgeons in the UK in 1983" or "2020". So you got an idea of what was happening at one particular time.

This was quite important because we became very concerned about unnecessary use of blood once non-A, non-B in the late 1970s became known about. There was a mandate -- not a mandate -- a suggestion from most blood transfusion doctors that if you only need to give a patient one or two units of blood, you probably didn't need to give them a transfusion at all and that you could protect them from this risk. This was only evident in the more recent years in transfusion medicine, whereas back in the 1970s, or so, people or doctors would transfuse their patients with relatively small amounts of blood which probably wasn't necessary. They could just have clear fluids, which didn't carry any risks.

So that's how we avoided the bias of going to one surgeon. The NIH PubMed is a much better way of doing it.

Q. If that research showed not that transfusion was usually required in the majority of cases, or indeed a near certainty, but that transfusion was not

generally required, but could -- obviously depending upon what precisely happened during the surgery -- from time to time be required, what would the approach be to that? Would that be sufficient, coupled with perhaps evidence from medical records that there had been some form of surgery, or did you require there to be positive evidence that most such operations would involve transfusion?

A. Well, we were interested in a percentage that required blood transfusion because don't forget our mandate -- we were implementing recommendations that had to be probably, which meant in legal terms, I gather, that it was more than 50% likely that any occurrence had occurred. With that constraint -- one of the reasons we went to the publications in NIH PubMed was there was, you know, objective quantitative data. You know, a surgeon would like to be -- would say "Well, all the bowel resections I have done" and there are maybe 150 in a surgeon's life with one particular operation, he would have recorded, possibly for an MD or an MSc that only 70% of these required blood transfusion, in which case we could authoritatively sign off on that. But it might say "only 3% required blood", in which case we would be less likely to agree that.

All the time, of course, we knew that the

appeal group could actually say "No, we find we should give the patient the benefit of the doubt". The appeal group were operating to different rules. They were told that whatever they decide was absolute. We knew that what we decided was going to be reviewed by an appeal board, and we didn't want to be either positive or over-negative. We tried to implement the rules as we saw them. In other words, if there are definite notes in the case notes of a transfusion, that was fine. If the patient had a history of intravenous drug use or had received a transfusion abroad, as well as one in the UK, it would be more likely that the one or the behavioural problem were the cause.

I will give you an example, for instance. In Egypt, after the attempt to eradicate schistosomiasis, something like 20 to 30% of the Egyptian population were hepatitis C positive. So if we heard, as we did in one case, that somebody had had an operation in Egypt, it was more than likely they had had infected blood in Egypt.

The other information we tried to integrate, by the way, which I should mention here, was what genotype of the virus was involved. You probably know from earlier people that there are maybe five or six

genotypes, which is a variant of the hepatitis C virus and the prevalence in different countries is markedly different. If I remember correctly, genotype 5 is common in China and if the patient had lived part of his life in China and part in Britain, whereas the common genotypes here are 1 and 3, and the patient had genotype 5, we would conclude that it is likely to, on probability, to have been acquired by something that happened in China.

So all that sort of information had to be integrated and a decision made with a safety net mentioned in the letter that if the patient felt strongly, or felt at all, that he had been disadvantaged, then he or she could say, "I'd like to go to appeal", and Nick Fish would actually suggest that they might want to look at the genotype in these type of issues to see if that information could be presented, you know, to help the patient's case.

That's all I can say on that but we recognised it wasn't ideal but combined with the appeal process we felt it was not going to disadvantage the patients if we were -- if we applied the rules as they were mandated to us.

Q. If I can just go back to the evidence that you might look for through the published medical material. You

gave us two examples, one of evidence to suggest that in only 3% of cases a transfusion for a particular type of procedure might be required, the other that in 70% of cases a transfusion might be required.

Did you need evidence of transfusions being used in more than 50% of cases for a particular procedure, in order to be satisfied without there being supportive evidence in the medical records?

A. Yes. I mean, they tended to be very polar. I mean, you know, most operations were things like cholecystectomy and tonsillectomies and, you know, very few, in single figures, would require transfusion there, whereas as trauma, cardiac operations, you know, in the early days, would require a transfusion in the majority of cases.

I mean, just to give another example to illustrate, for instance, more recently during liver transplantation some surgeons managed to do the liver transplant without the requirement for any transfusion. That was related by a blood-saving technique where they aspirate the blood that is spilt into the wound, wash it and put the red blood cells back.

So, you know, that's why I make the case of -- you know, with leeway we tried to get a view at one

point in time with a particular operation what the probability was, but I would be misguiding people if I said, well, you know, I can tell that by 49% refused, 51%, you know, let the case go through. It would be plus or minus, you know, maybe 10 or 20%. I could justify that in my own mind by the fact three or four other people would then look at it at the appeal process.

Q. We can take that down.

Mr Fish accepted yesterday that there might be three problematic consequences of pinning too much faith on the appeal process and I just want to explore those with you and see whether you have got any comment on it.

The first might be that some people, very ill with hepatitis C, for example, suffering depression, suffering brain fog and the like, might not go to appeal. They might feel there is no point. They might feel too ill. Not all refusals were appealed. The Inquiry has seen examples, for example, of somebody who had dyslexia and felt he couldn't go through a further appeal process. So would you accept that would be potentially a problem, that some people might just give up at the first stage?

A. Yes, I mean, undoubtedly that could be a possibility.

I would imagine that's quite rare. Most people -- I don't have the figures in front of me -- a large proportion of patients did go through to appeal, having been initially turned down.

Q. The second potential problematic consequence of pinning one's hopes on the appeal process would be it is requiring people who, as I say, may already be very ill, debilitated, to go through not just one application process but to go through a second process as well, which might in itself take a toll on them. Would you accept that?

A. Yes, I would, of course. It is worthwhile looking at the figures that you have later on in your data. I think you say there is 6,712 patients who applied for a stage 1 application, approved at first stage 5,529, you know, which is 80%. So, you know, not that -- you know, we waved through a large number. Whenever the issues of patient feedback were put before either Skipton or Caxton, it was always apparent that complaints were looked at very carefully but nobody ever looked at the proportion of patients who thought their case had been handled very well. That's 80% according to these figures.

I think the figures of stage 2 applicants that thought that their case was handled quite well, or

even very well, you know, was high. So I wouldn't want you to present the view, you know, that the system was absolutely, you know, useless and rough riding over people's views, really. I think that would be wrong.

Q. I am simply trying to --

A. Undoubtedly, there were holes in the system. There were less holes in the stage 2 process that doctors were involved in deciding, not because we are any better than anybody else, but stage 1 was an almost impossible task and, when you add the special care mechanism to it, it became a terrible situation.

Dr Main, who was involved, when it was transferred to the NHS business with me, we took the view that if the patient's GP and/or the hospital doctor said that the patient's depression and brain fog were due to hepatitis C, we said "Who are we to gainsay that?" We signed all those off, probably to the annoyance of whoever had to pay the bill.

So, you know, we had to work with a mandate. We had some input into deciding who got what, in other words what the criteria were, but if some criteria were put forward that we couldn't operate, however much goodwill we put into it, you know, what do we do? With the special care mechanism we waved through most

people and that was partly because of our own experience. Dr Main, myself and Geoff were fully engaged in research into viral hepatitis, particularly this type, and we always tried to bring to the table the most modern research, which often resulted in us changing our view from maybe five years ago.

So we tried to keep it up-to-date. We did the best we could and recognised that it was far from foolproof, but we didn't design the system, other than the stage 2 system.

Q. Can I just ask what your policy or approach was in relation to cases where there was some evidence or suggestion of intravenous drug use?

Mr Fish told us yesterday that he was told when he was learning the job, essentially, that that would always be a more likely route of transmission than transfusion, and that was then effectively his approach, so that intravenous drug use cases would be rejected.

Did you have much involvement in cases involving suggested intravenous drug use?

A. I think the background information to that is that if you look at populations of patients who are intravenous drug users, then you will find it is virtually 100% have hepatitis C. So if there was

a well validated history of intravenous drug use, you could virtually be certain that that was the cause of their hepatitis.

I mean, the other figure you need to know is, of the total population of hepatitis C cases that Health Protection England reviewed every year, although the percentage acquiring it through blood or blood transfusions or non-intravenous drug methods maybe a decade or two decades ago would be maybe 30 -- 30% or so were due to transfusion, but in latter years it is virtually that everybody, or greater than 95%, are due to intravenous drug use.

It is not sufficient, when you are trying to elucidate the story of the drug users, to just ask the patient in a clinic once "Did you use drugs?" Nobody wants to admit that. But one of the aspects of being a doctor, and a liver doctor interested in viral hepatitis, is you soon learned that you had to gain the patient's confidence, and you -- you know, at the first consultation you might ask if you used drugs and they would say "No", but after four or five returns and follow-up clinics, they would say "Well, actually, as a student once I did use them". And, you know, just once is enough. Because, of course, who -- I am digressing now I suspect, but, you know, when you are

at a party and somebody says "Would you like drugs?", I mean, who is offering it but somebody selling drugs who will have been using themselves. So they are almost certainly giving you a needle system, because your mother doesn't give you a needle to go out with when you go out to a party. You will be actually using a drug provided by somebody selling drugs and you will become infected. So almost synonymous with hepatitis C, outside the context of blood transfusion, a positive result is indicative or highly likely that that patient at some stage, past or present, has used drugs. And that's why that -- what Nick Fish said, I suspect why he said it.

Q. I understand that was policy and approach of the Skipton Fund. Did you yourself have involvement in deciding IVDU stage 1 applications as far as you can recall or were you generally only called in for review when there were clinical judgments to be made?

A. Oh, no, I was involved in judging stage 1, yes.

Q. But were you involved in rejecting applications on the sole basis that there was evidence of IVDU?

A. Certainly some. I don't know whether it was all of the ones I saw, but certainly some of them.

Just go back to the figure. 6,712 stage 1s, of which 5,519 -- or 29 -- were passed through. You

know, no -- just on the basis of the paperwork. So we were all focusing on -- you know, I think 1400 of the cases, which is less than 20%, where one had to decide, on the basis of no written evidence of blood transfusion, what the other possibilities were. And that's where Nick would look at them first, then I would, and then on occasion all three of us would have looked at it. And you ended up by saying, "Well, it is a possibility it was a blood transfusion, but we can't be certain. Let's pass the ball to the appeal group."

Q. Can I ask you next about another category of cases? These are cases where the infected person was deceased. We have looked already at the issue about trying to determine cirrhosis for stage 2 purposes, but if the question was, for example, for the purposes of a bereavement payment, whether hepatitis C made a cause or contribution to the death, were you involved in assessing those applications?

A. Where hepatitis C was a cause of contributing to death?

Q. Yes.

A. Well, I am sure I must have been, because that would be -- you know, I mean, I think probably Nick Fish and Geoff and I would all have discussed those sorts of

cases. That's why, in the end, we came up with that formula that I mentioned earlier where the mortality rate of mono-infected and dual-infected people, which I think was in Nature or something like that, a highly respected journal, and that provided wonderful data which allowed us to come up with a formula.

Q. I am going to move now to the Caxton Foundation. You were involved with the Caxton Foundation from 2011 onwards. But I think this is right, you didn't sit on the National Welfare Committee, so you weren't involved in decision-making about individual grant applications?

A. No, no. I was allocated to the audit committee, which -- a gentleman called Thomas, another Thomas, and I sat down once a year with the audit company -- I have forgotten who they were -- just to make sure that it all stacked up. Because following the fraudulent episode that occurred in the -- I think I have forgotten which one -- that was the Macfarlane, wasn't it?

Q. No, the Skipton Fund.

A. Yes -- yes, we were all aware of the need for audit, so -- and it was apparent that I had medical knowledge but not much else that was useful to the Caxton. So I didn't -- I then got transferred across to the

Skipton.

Q. So in terms of your involvement with the Caxton Foundation, is this right: it largely involved just attending the trustee meetings?

A. Yes.

Q. And contributing to general discussions about policy?

A. Yes.

Q. How often were you called upon to provide medical information to either employees or your fellow trustees at Caxton about hepatitis C?

A. When I was appointed to Caxton, I was conscious of the fact that I didn't have a heck of a lot to contribute, as I say, because it was social aspects and Department of Work and Pensions were involved. So I offered to give a presentation, really, on -- really, a bit like the thing I prepared for Penrose and I think you have cited in some of your paperwork. I had a nice set of slides for that. So I did a presentation.

And when Geoff Dusheiko joined us, he updated that on the newer methods of treatment. So, you know, we were looking, in the context of Caxton and Skipton, as how we could contribute really.

Q. Can I ask you to look at one set of minutes? It is at CAXT00000109_105, please, Soumik.

SIR BRIAN LANGSTAFF: There is something wrong with your

number of zeros.

MS RICHARDS: I have too many zeros in it. It is CAXT0000109_105. Thank you, sir.

So these are the minutes of a meeting of the board, 1 November 2012. We can see that you are present there.

If we go to the third page, please, Soumik, we can see there is an overall heading "Regular Payment Scheme". Then if we go just a little further down the page, we can see a paragraph beginning:

"Professor Thomas suggested ..."

So:

"Professor Thomas suggested a plan to contact the 12-15 Haemophilia Clinical Specialists in the country to help 'advertise' Caxton to their patients. It was noted that not all these patients would be eligible but it was a worthwhile starting point. The Board agreed that Professor Thomas should discuss this with the ICEO to further inform the communication strategy."

Now we know from other material we have looked at, Professor Thomas, one of the issues for Caxton was it had a relatively low number of registrants in the early years. Fewer people were applying to be registered and to receive assistance from Caxton than

had perhaps been expected and an issue arose for the board about how to make people more aware of the existence of the Caxton Foundation. This suggests you had suggested making contact with perhaps haemophilia centres or haemophilia specialists. Can you recall whether that was taken forward?

A. What does ICEO stand for?

SIR BRIAN LANGSTAFF: Interim Chief Executive officer.

MS RICHARDS: It is, yes.

A. Interim chief -- was that Jan Barlow?

MS RICHARDS: There was a temporary officer. After Mr Harvey stepped down and before Ms Barlow was appointed, there was an interim chief executive officer, and that's what that refers to.

A. Yes. I don't recall what happened as a result of that. The reason I said that was that I was very impressed, through my work at the Royal Free, and with Professor Kernoff particularly, who tragically died, with how integrated a national structure the haemophilia specialists grouping was. And if you wanted to reach specifically the haemophilia population, then that would be the vehicle for doing that. But I didn't have any suggestions as to how you would reach those that had had blood transfusions or blood products other than Factor VIII or IX

concentrates.

I think that was the challenge to the system. That group of people were -- the only way of doing that would be through the Blood Transfusion Service. I guess that was the look-back service -- or study that was done. I don't know when it was in relation to this, whether it was before or after, but that would be the way to do that.

The other thing that was discussed at this meeting was, you know, how much there was a need for this, because there were several programmes on the television, Panorama and the like, and I don't think there were many people who had had a blood transfusion in the UK who hadn't seen one or other of these programmes. You might say how do I know that. I don't know that, but I think -- you know, they were shown on prime time TV many times. So I wasn't quite so concerned about that.

Q. Did you have any understanding from colleagues in the world of hepatology, any understanding of how well-known the existence of the Caxton Foundation was?

A. I think the hepatology nurses served a very useful function actually. They got to know the patients very well. I am talking now about the non-haemophilia patients, the ones I was talking about earlier, and

the haemophilia services in the specialist centres also had a very close relationship with their patients, because they were patients from, you know, a few years of age right through to adult life and old age.

These nurses, I think -- the haemophilia service developed this first, but one of the things I helped develop was the formation of hepatology nurses, and we employed several in our unit at St Mary's. These people certainly raised the attention of the patients to the Skipton and to the Caxton -- more the Skipton than the Caxton I think, probably -- and would help the patients fill in the forms. Because a hepatology nurse was able to do it as well as the doctors.

Q. We can take that down now.

Were you ever asked to provide advice to the Caxton Foundation about the impact of the various different treatments for hepatitis C and in particular the impact upon an individual's ability to work and earn a living during treatment?

A. No, I can't remember what was in the slide set that I used, but Dr Dusheiko actually gave a lecture when he joined, which was about 2015/16 sort of a time, and he had masses of data, really, on the results with the

various drugs. I'm not sure what else he included in that from memory I'm afraid.

Q. Now you have referred in your evidence earlier to the concern you had about the access to the new forms of treatment. I just want to look at the letter you wrote to the Minister on that issue.

It is WITN3824008, please, Soumik.

We can see it is dated 1 November 2014. It is from you and you say:

"Dear Minister,

"I am writing as a member of the Caxton Board and the Medical Director of the Skipton Fund, both involved in supporting those with hepatitis C acquired through receiving infected NHS blood or blood products."

Then you explain a little about the stage 1, stage 2 process. You say in the next paragraph:

"Around 90 patients receiving Skipton stage 1 payments, progress to cirrhosis each year. Once this occurs the cirrhosis cannot be reversed even if anti-viral treatment is successful.

"In the last few months orally administered antiviral drugs which are curative in over 90% of cases, have been licensed and are currently being considered, but not yet recommended, by NICE. These

drugs stop progression to cirrhosis thereby removing the risk of death from liver failure or HCC. The department has made these available to 500 patients on liver transplant lists and I am writing now to bring to your attention the fact that in the coming year 90 patients receiving ex gratia Skipton stage 1 payments, will develop irreversible cirrhosis which can be prevented by rapid access to these drugs. At Skipton we are aware of these cases and feel that you would also wish to be made aware of the problem so that you may consider whether these cases, where the NHS has accepted responsibility for their HCV infection, might also be considered for fast track access to these virtually 100% curative -- but very expensive -- antiviral drugs."

Did you receive, as far as you can recall, a response from the Minister or from the Department of Health to this letter?

A. Yes, we did. Of course I haven't got a copy of that, but I wrote as a member of the Caxton board and I took it to the Caxton board to make sure that they were agreeable to me sending this. And Jan Barlow was the chief executive at that time, and I have forgotten who was the chairman of the meeting, but they said yes, that I should send it off. And I think the reply came

back to both of us, so it should be in the notes, but essentially what -- I think what was said was that they didn't want to -- the Department of Health didn't want to give preferential treatment to one group of patients rather than to another and that all should be treated equally and come through the NICE system, where -- and made the point that, whilst I was saying that this group should be given prior access because things could go wrong, as they went from Ishak 5 to Ishak 6, as we were talking about earlier, and detectable by Fibroscan, these people, since it was now a NICE-recommended treatment, it was mandated by NICE they should be treated I think within three months, but I couldn't remember what the NICE criteria was or is. I think it is that NICE-recommended treatment should be available within three months. You probably know that or can find it out.

Q. Yes.

A. And that this would cover this issue.

Q. Yes. I think that was perhaps a little later in terms of the chronology of events, but is this right: your argument that perhaps there should be a fast-track access because these were people who had been -- whose infection was the responsibility, in a broad sense at

least, of the NHS, that particular argument fell on deaf ears?

A. Well, no. I think the Minister said that it was covered off by the rules and regulations covering NICE. This was by that stage -- not yet recommended by NICE. But if it wasn't recommended by NICE, then the NICE rules wouldn't be relevant. This was quite some time ago and I can't remember the detail of it. I remember it didn't come about, really, is what it amounts to.

Q. I just want to ask you a little next about the special category mechanism and the discussions that you were involved with in relation to that. If we could go to DHSC --

A. By the way, can I just say that letter really followed on from that debate that we had earlier about what was the crucial cut-off for cirrhosis with Fibroscans, and it was one of the reasons -- I am fairly sure it was one of the reasons why I wanted to go for the lower level, because I thought that would be another way of skinning this particular cat and would include that group, the Ishak 5s, which are just the pre-cirrhotic group.

Q. I am going to ask you about the Special Category Mechanism. I think they were originally referred to

as an individual assessment model or a health impact assessment and then became known as the Special Category Mechanism. If we could just pick it up at CAXT0000094_145.

There are multiple documents referring to this issue, so I don't want to go through all of them. We can see here these are parts of a meeting of the Caxton Board on 15th February 2017. If we go to the next page and look at the bottom of the page, in the penultimate paragraph, beginning "The board noted", we can see reference to the Special Category Mechanism:

"The board noted that CP, HT [that's you, professor], MK and JB continued to be involved with the Department of Health Reference Group."

There is reference to meetings having been cancelled:

"The Special Category Mechanism ... had been the main agenda item at recent meetings, but JB reported that progress had been slow because the criteria for this were being driven by DH's attempt to counter the legal challenges."

Then there is reference to:

"... a further draft of the SCM, which the Group had agreed was probably the best it could be in the circumstances."

Then you are recorded as saying this:

"... HT advised that the SCM eligibility criteria were still very subjective and would be difficult to assess."

What was your concern in that regard?

A. Well, this stemmed from work I had done with Daniel Forton and Simon Taylor-Robinson, looking at whether hepatitis C affected the brain. We were able to isolate in the brain a virus variant of hepatitis C, which was the regulatory element which controls replication of the virus, from -- the one we got from the brain was different from the one that was in the cripple blood, indicating that it was a functional virus working in the brain. Therefore I was convinced when we did SF36 studies that was the observation that we had made with Graham Foster and others that depression and cognitive changes, what became known as brain fog, were caused in a proportion of the patients by hepatitis C.

The virus was in the brain and when we did comparative studies of quality of life between hepatitis C and hepatitis B as a control, these two areas, depression and brain fog, cognitive defects, came out as significantly different and associated with hepatitis C.

So I felt that they should be taking some -- we should be trying to dissect this away from the large proportion of patients who had depressive problems and even cognitive abnormalities in the general population unrelated to hepatitis C, and it would be impossible to differentiate these two.

Having set up objective criteria for stage 2 payments, which I think in retrospect were shown to work quite well, and worked through at the time with stage 1, found it very difficult to be objective in this group, and to add this to it, a Special Category Mechanism, which allowed additional payment or significant payment for people who had depression and cognitive abnormalities would actually mean that virtually everybody would have them. It turned out to be the case: virtually everybody applied for this, if you wanted to be cynical, assuming that they were depressed and assuming that their depression was related to their infections. Not unreasonable, you may say, but a significant proportion of people, of course, in the general population have depression and it is reasonable to assume that this proportion of people with hepatitis C had the problem before hepatitis C infection occurred.

So I didn't relish the fact of trying to make

this work, to be honest, and I wanted the reference group to try to work towards more objective ways of dissecting out whether these problems were related to hepatitis C or not and they weren't forthcoming.

So yes, I wanted the SCM to go through, but I didn't want it to be another situation where we really couldn't define the group where it was due to hepatitis C. So when the NHS Business group took over and this SCM was put into effect, Janice Main, a colleague of mine, and I, used to go into Skipton House before the NHS Business guys took all this up to Newcastle. We sat down and tried to look at hundreds of these cases coming through and we decided we couldn't differentiate them and that if the GP or the hospital consultant or a nurse said that this was -- well, they were given three choices. It was improbable it was related hepatitis C, which think only three people ever ticked out of hundreds, and it is possible and probable.

So we gave everybody where it was said to be possible and probable the tick for the payment because we couldn't say one way or the other. If you like, you may say we learned from our previous experience with stage 1s. You know, in this subjective environment you have to assume that the primary care

physician, the GP, or the consultant or nurse involved in the hospital care of that patient, would be in the best position to assess the patient, and if they said it was probable, then the payment should go through.

But, you know, we had already given out very large sums of money, I think over 300 million and I felt we should try to be as objective as possible, but this was impossible. So I felt at least I had to say at the reference group that this was the case but I didn't have a better suggestion really of how we could differentiate.

Q. Then the reference group, as well as considering the Special Category Mechanism, considered other aspects of what the new Business Services Authority scheme might include?

SIR BRIAN LANGSTAFF: Just before you go there, can I ask this: how did you judge being related to hepatitis C, because "being related to" may mean a number of different things?

A. Yes. I take your point. It may be causatively related or it may just be associated with.

SIR BRIAN LANGSTAFF: If causative related it may not be the only cause but may be a contributing cause.

A. So it would be relevant whether the patient had depression or cognitive problems beforehand. If

hepatitis C could make it worse, that would be enough to make the payment as well.

SIR BRIAN LANGSTAFF: That would follow legally in a case in which there was a question of whether the condition for which compensation was being sought had been caused by what is generally a multi-factorial condition.

A. I think later on I mentioned Koch's postulates. I think Koch was a German infectious diseases or epidemiologist. Koch's postulates say that before an infectious agent can be thought to be causatively related, which I appreciate, sir, that this is different to what you are suggesting, you are just saying it could be exacerbated by hepatitis C --

SIR BRIAN LANGSTAFF: I think the expression I would use is "cause or contributed to".

A. Right, well, Koch said that for an agent to be causatively related it should be found with the disease or the symptom and when the virus or bacterium or fungus, whatever, is cleared, then the symptom or illness under consideration should disappear. In other words, it came on with the infection and then went away when the infection was cleared.

We tried to think about using Koch's postulates in relation to this particular problem because, of

course, virtually 100% of people with hepatitis C can be cured. So there was a possibility of looking at which of these problems got better when the virus was cleared, in other words the second component of the Koch's postulates. The Americans particularly said that a lot of the depressive and cognitive abnormalities, which were measured by instruments called SF36, which just was a series of questions, I think there were 36 of them, hence the name -- and specialist variants of that where you could do serial measurements before and after treatment.

The Americans argued that most of the symptoms didn't go away after the virus was cleared, but it turns out we were doing some studies with magnetic resonance spectroscopy. It is a sophisticated system that looks at various molecules in the brain. We found, originally, that in HIV and in hepatitis C stage 1 there was a sub group of patients who had this particular pattern, which suggested there was a change in the brain. It would have been possible to use these scans, which cost a couple of hundred thousand pounds each to do -- they were a research programme -- to tell whether individual patients had these characteristic changes which we saw initially in HIV but were also present in stage 1 hepatitis C, which

I think would have differentiated the virus caused ones from the other causes, depression or brain fog, that is unrelated to hepatitis C.

But it doesn't answer your question of whether it is causatively related or contributed to. I don't think you can differentiate those, except by looking retrospectively as to whether it got better or partially got better when the virus was cleared.

SIR BRIAN LANGSTAFF: Well, I think the magic of the phrase "caused or contributed" means this covers both. You don't actually have to differentiate between the sole cause or one of a number of causes or contributors to a condition.

A. Yes. Many conditions are caused by many for factors. Of course, they can operate in conjunction with each other as joint causes, yes. I take your point. The bottom line is that we gave the SCM payments to virtually everybody who applied for that very reason.

The other group that we thought should be given be these payments were people who during their stage 1 illness had been treated with interferons, which initially, I thought, wasn't justified, but experience in reviewing these with individuals it clearly became evident that many people did have the interferon-related side effects.

When you took care of patients going through those interferon treatments, it wasn't surprising that their memory had a long-term compromise, really. And also, if they had rheumatoid arthritis or myxedema, a thyroid condition, these were also made worse afterwards. So I changed my view during that process, you know. And when the SCM issue came up, we thought that virtually anybody who had had interferon should probably get these payments, because there was a correlation -- maybe not causative, but a correlation -- which, you know, might mean it was related to, albeit not in the Koch's postulates way. So I don't know if that has helped at all.

MS RICHARDS: If it assists -- and, sir, we will no doubt look at this when we look at the current schemes in May -- but the current Special Category Mechanism application form, which I looked up this morning, poses the question in this way of the clinician or nurse:

"In your opinion how likely is it that your patient's mental health problems are attributable to the hepatitis C infection or its treatment or effects?"

SIR BRIAN LANGSTAFF: It is the same question.

MS RICHARDS: It is, although the four potential answers

are:

"Not likely explained by other causes.

Possible.

Highly likely, and

Definite."

There doesn't appear to be a box for "likely". But that's a question for the future rather than for Professor Thomas.

Just before we break for lunch, professor, I just have --

A. I just want to know -- is it possible to ask what proportion are getting SCM payments? I think it is virtually 100%, isn't it, of stage 1s, or is it?

Q. I think we will be in a better position to know that, Professor Thomas, when we examine the evidence in May.

A. Sorry.

Q. I just have one further question about the reference group discussions, not on the Special Category Mechanism but on a different aspect of the discussions.

If we could just look at DHSC0046884_020, you will see it is a reference group meeting, 16th November 2016.

Again, there is a discussion about the Special Category Mechanism. I am not going ask you further

about that.

If we could go to the last page, we can see the last heading is about "Policy for £10,000 payment [of] the bereaved". Then it is said --

SIR BRIAN LANGSTAFF: I think it is probably "to the bereaved". The T and the O are transposed.

MS RICHARDS: I think it probably is "to the bereaved", reversed to O-T. Then it says:

"For the purpose of the proposed policy the intention is that you qualify as 'partner or spouse' of the deceased registrant/primary beneficiary if either of the following applies."

Then there is a provision as to what amounts to a partner or spouse."

Can you recall, Professor Thomas, whether there was any discussion within the reference group of widening the category of people who could receive the bereavement payment to categories of relatives beyond partners and spouses?

A. I can't really -- I ended up at one of these sort of meetings with -- as one of the only -- well, we're usually the only medic present focusing on those issues, really, and I'm not sure I picked up on this. No, I can't shed any light on that, I am afraid.

Q. We can --

A. Hold on. Yes, I think that was mentioned. Did that happen or did it not happen?

Q. I am just asking you whether you have any recollection of discussions about it. We can pick up what then got translated into the scheme with the relevant civil servants in due course.

A. No. The other issue that was raised here was whether hepatitis B was mentioned. I know that one or two people mentioned that but I can't remember what the outcome was to be honest.

Q. You anticipated what was going to be my final question before lunch, Professor Thomas, which was just about hepatitis B.

Can I put it more generally than relating to specific conversations within the reference group that you may not recall?

Work on hepatitis B has formed a significant part of your career over the years. Was the exclusion of people infected with hepatitis B from the Skipton Fund and Caxton Foundation something that ever came up in any of the discussions or meetings you had over the years with the Department of Health?

A. No. I think it was mentioned at the reference group. As I say, I couldn't remember what the outcome was. I think it does seem an anomaly that hepatitis B

didn't feature. I felt that the hepatitis B population -- this is -- what I am going to say is not really relevant to those haemophiliacs and those who received hepatitis C through a blood transfusion, because don't forget I said earlier, about 95% of my patients with hepatitis C were intravenous drug users. And they deserved good treatment just like everybody else but there was a stigma attached to that group of patients. And my nurses and my staff gave these guys expert care and they were very difficult to manage. The hepatitis B patients were cross-stigmatised, if I could use that phrase, because people didn't differentiate between hepatitis B and hepatitis C.

Most people with hepatitis B were Asian, Chinese in particular, where 10 or 15% of the Chinese population were hepatitis B positive. They had acquired it from their mother at birth. They often were very sheepish coming to the clinic, because they thought all viral hepatitis was related to intravenous drug use.

Saying that, I spent a lot of my life looking after people with intravenous drug-related hepatitis C. So I am not saying they shouldn't have required it, but I did think the hepatitis B patients were left out, if I am making the point properly. You say

I spent a lot of my life working on hepatitis C, but I spent all of my career -- well, the majority of it, except for the last couple of years -- working on hepatitis B. I think it should have been much more to the fore in some of these schemes. Some haemophiliacs did get hepatitis B.

The other thing to point out, though, in relation to hepatitis B and hepatitis C, if you got hepatitis B as an adult or even as a toddler, as many haemophiliacs did, then you had an 80 or 90% chance of getting a circumscribed acute episode with recovery, whereas the converse was true with hepatitis C. 80% got chronic infection and all the downsides of risk of cirrhosis and what have you, and liver cancer, related to the chronic infection. So I think that may have been part of the explanation, although not the justification, of why the hepatitis B group were left out, really, but they used to come to our joint hepatology clinic that we ran at the Royal Free with the haemophilia group there with Professor Kernoff and co.

MS RICHARDS: Sir, I note the time. I am going to move on from the financial support schemes now to ask Professor Thomas some more general questions relating to hepatitis. So perhaps we can pick that up after

lunch?

SIR BRIAN LANGSTAFF: Let's do that. So we will take a break until 2.05. 2.05, professor.

A. That's okay. Yes.

(1.04 pm)

(Lunch break)

(2.05 pm)

MS RICHARDS: Professor Thomas, I am going ask you next about some aspects of your early involvement with issues relating to non-A, non-B hepatitis and hepatitis C.

If we could go, first of all, please, Soumik, to RLIT0001242.

You will see, Professor Thomas, this is "Unresolved problems in Haemophilia". And if you go to page 3, we can see these are the proceedings of an international symposium held in Glasgow in September 1980, and you are one of a number of speakers and attendees.

If we can then go to -- let's find the page -- I think it is page 33, Soumik.

We can see this is a short paper authored by you, Dr Bamber and Dr Kernoff, "Clinical, immunological and histological aspects of non-A, non-B hepatitis in haemophiliacs". I may come back to

a couple of your publications around this time in a little while, but we can see this is the paper presented at the symposium.

What I want to do is take you to the discussion at that followed the presentation of the paper. We can pick that up at page 42. We can see a question being posed by Professor Stewart about active hepatitis and the question is posed, in particular:

"What happens in the haemophiliac?"

We can see your answer, and you say this:

"The lesion of chronic active hepatitis, is a progressive lesion, and one would, in a proportion of these patients, expect an element of fibrosis, and ultimately cirrhosis. None of our patients has had cirrhosis, but then, if we are to believe that this illness at the most has been going on since 1974 when the commercial concentrates from first introduced, then this period is short in the course of the disease. There are some indications that these patients may have lesions which will turn to fibrosis or cirrhosis."

Then you set out various observations and measurements.

Then if we pick it up in the last six lines of this page, you say:

"It is really now a question of how long ... just because we have not seen it in this six-year period, it does not mean that it will not happen. I think the thinking is that it takes ten or twenty years, or even thirty years, for these lesions to progress. I think we have to realise that these are young patients, with many years ahead, when we are considering the significance of these lesions."

Then you go on to contrast that with the situation in relation to chronic persistent hepatitis, which would have a much better prognosis.

Can I just ask you, first of all, whether -- can I put it this way? What you appear to be saying here, if I can paraphrase and if you can assist with whether this is correct or not, is, although you are not currently seeing levels of cirrhosis in the patients whom you were concerned with and whom you had been studying, your suggestion here was that was not because that was not going to be a problem in the future, but simply a reflection of the progressive nature of the disease, and your expectation was that there would be problems with chronic active hepatitis, fibrosis and cirrhosis in the future for this cohort of patients. Is that a correct understanding of the message you were giving here?

A. Yes, I think that's spot on, really. I mean, it was one of the reasons for doing biopsies, because we knew by analogy with chronic hepatitis B that if you saw chronic persistent hepatitis, where the inflammatory calls were in the portal tracts and not going into the rest of the liver, then this was essentially a benign condition, whereas if you saw, as the name implies, chronic active hepatitis, then this -- the liver cells in and around the portal tracts would be destroyed and would be replaced by fibrous tissue, which would ultimately result in nodule formation and bands of fibrous tissue, which we call cirrhosis.

So the initial biopsies suggested that chronic persistent hepatitis predominated and that chronic active hepatitis then occurred, and that then went on to cirrhosis.

I tried to demonstrate what the current thinking was at any point in time by Sheila Sherlock's book, which I think you mentioned somewhere else, or I presented to the Penrose Inquiry, which showed that -- in one particular edition she was saying -- she is the doyenne of liver disease -- dead now, of course -- which at one stage, in one edition, the earliest edition, I think '74 or something like that, she was saying, "This is a mild condition and we don't

have to worry too much", and then in the next edition, when these biopsies had come through, she said, "Ah, chronic active hepatitis, this is likely to be progressive."

So, yes, you're completely correct, that the presence of chronic active hepatitis was a bad prognostic sign, and that as with hepatitis B, this develops over decades rather than months or years or small numbers of years.

Q. Then just to pick up the next -- no, I think two papers on from this, Professor Preston and others' paper.

Page 45, please, Soumik, of this.

This is a paper presented by Professor Preston, Dr Triger and Dr Underwood. Again, if we go to the discussion, it starts on page 50, and I wanted to pick up your contributions, which begin on page 51.

If we look at the bottom half of the page, you say this, picking it up I think three lines into your observations:

"I would suggest that we are at a stage now where we have got an idea of the sorts of lesions that we are seeing. A significant proportion, perhaps 40 or 50%, have chronic active hepatitis."

Then there is a reference to the analogies with

hepatitis B. You say:

"It is much more likely that this form, since it is presumed to be caused by a virus, will be more closely analogous to the hepatitis B form of chronic active hepatitis ..."

Then if we just go to the bottom of the page, you then refer to:

"An alternative approach is to observe [the patients] for longer ..."

Then you say this:

"We are studying the patients fairly early on, perhaps 2 years or so at the maximum after onset of illness, and we are not seeing much in the way of fibrosis, whereas Dr Triger is studying it perhaps a few years further on and he has got a significant incident of cirrhosis. So it may be a progressive lesion."

Then in the next paragraph you give a further reason for feeling this may be progressive.

Then you say in the third paragraph:

"One can predict that there will be problems in the future."

Then you pose the question: should there be trials being done or do you follow the patients for longer?

Then if you can just, before I ask you to comment, go to page 58. Bottom of the page you say this, in the last four lines:

"As Dr Triger has said, it is in 10 years time that we shall see the problems. Bearing in mind that the proportion of the patients that are infected, or have persistent abnormal liver function tests, anything from 60 to 80%, it will be an enormous problem when it happens."

Again, can you just assist us with what your concerns were when you said "it will be an enormous problem when it happens"?

A. Well, because a large number of patients, both with coagulation abnormalities, like haemophilia, and also the substantial number of people who we thought were out there who had been infected because of blood or blood transfusions, this cohort -- and we guesstimated -- and by we, I mean the epidemiology community and the Health Protection England guys and girls, they were predicting there would probably be 150,000 to 200,000 people with chronic hepatitis C out there, and if this was progressing then we were going to end up with quite a lot of people with cirrhosis. And I knew that cirrhosis, as did David Triger, had a significant mortality.

In fact, the percentage with cirrhosis, I always remember it by saying: every ten years there is another 10% who have cirrhosis. So, you know, when some of the young people -- for instance, there was a haemo plasmapheresis cohort in Germany who got infected because of infected plasma, you know, when that group of people, who were several hundred I think, would work through, then up to, you know, 20%, 30% would have cirrhosis. And a significant number of those, as I have said, who were -- 2% to 3% per year at risk of liver cell cancer. And, something I haven't mentioned yet, 2% to 3% per year die of liver failure and require -- the only treatment for that is liver transplantation. So add all these things up and it looks like a big problem on the horizon, not to mention the problem from the patient's point of view, because cirrhosis is not a pleasant condition.

Q. So that's September 1980, that symposium. Then I want to just ask you a little about a paper that you and others published in 1981.

Soumik, that's RLIT0000497.

This is a paper which I think we haven't looked at yet within an Inquiry hearing. It's "Ultrastructural Features in Chronic Non-A, Non-B

(NANB) Hepatitis: A Controlled Blind Study". We can see from the bottom of the page it was accepted for publication August 27, 1981 and it was published in the Journal of Medical Virology in the course of 1981.

If we can just go up to the bottom of the page again, we can see what the study entailed:

"Liver biopsies from 12 patients with chronic non-A, non-B ... hepatitis, 7 with hepatitis B surface antigen ... positive chronic liver disease, 1 [hepatitis B] positive normal carrier, and 4 patients with non-viral liver disease, were examined by electron microscopy for cytoplasmic and nuclear changes."

Then if we look at the introduction just a little further down, you and your fellow authors say there:

"Following the development of diagnostic serological tests for hepatitis A and B infection, it became apparent that there were additional unknown viruses causing hepatitis in man and these were been named the Non-A, Non-B ... group ..."

So that's the background.

If we can go over the page, I am going to ask you about the first patient group that you describe, under the heading "Patients and methods". You say:

"Three patient groups were studied."

The first is those with non-A, non-B chronic liver disease.

Before I do that if we just look at the top of the page, just so we can understand the purpose of this study and this paper, which is about ultrastructural features, there's reference there to "ultrastructural alterations" being described in chimpanzees infected with serum from patients with non-A, non-B hepatitis.

What was the particular purpose of the blind control study that you were undertaking here?

A. Well, all patients really that came in with unexplained transaminase elevation in Dame Sheila Sherlock's unit would have a biopsy early on in the management to decide several things. Obviously, we would do serological tests to diagnose hepatitis A and B, without going to the extent -- which carried risk to the patient as well as to a lot of in-patient care, before going to a biopsy, which would tell us exactly whether this was acute or chronic disease, because you may have noticed that in haemophiliac patients with Factor VIII concentrates the transaminases go up and down. They will have periods of normal transaminases and then a week or so later the transaminase will go

up.

These patients came in with significant liver test abnormalities. The first thing we required to know was whether it was an acute episode, having excluded hepatitis A and B, or whether it was acute non-A, non-B, or whether it was already chronic non-A, non-B, with chronic active hepatitis, which would put the patient at risk of cirrhosis.

So the biopsies were done for diagnostic routine clinical care but other patients coming through the unit had had biopsies and the randomised part of it was looking at a group of patients from each of a series of designated or diagnosed diseases. So chronic hepatitis B is diagnosed serologically to assess what sort of liver disease they have in the prognostic episodes and the prognostic outlook. They would automatically get biopsies or routine biopsies. Similarly, patients with ALT abnormalities attributed to non-A, non-B.

The only way of determining what non-A, non-B might be due to is there were studies in the United States and in the London School of Hygiene here in the UK, showing that there were certain electron microscopic abnormalities found in patients with one particular type of non-A, non-B, which subsequently

turned out to be hepatitis C.

So what we wanted to do is to take biopsies where we knew the diagnosis, which was hepatitis B, and then take a similar number of biopsies, which had been done for routine care reasons and look at them all under the electron microscope really to see how many had these changes, which at least in animals, in chimpanzees, had been shown in the literature to be due to non-A, non-B.

It was a way, if you like, of showing whether this was one disease or several diseases and really trying to get at least on one basis a diagnosis. So that's why it was done.

It turned out that these electron microscopic changes, intranuclear particles and changes in the parts of the cell where proteins are made, called the endoplasmic reticulum, these were similarly present in human patients as they were in the animal studies, the chimpanzees, mainly from NIH in the United States but some done here in the UK, in the London School of Hygiene.

So it was really to see if we could get a histological basis for saying "This group have a type of non-A, non-B". At that stage the people in the United States said that there were two types of

non-A, non-B, with one with a short incubation and one with a long incubation. So to get some other basis for separating out the two, long and short incubation, we needed another marker. So this was a study, really, to look at that issue --

Q. Then if you --

A. -- and it turned out that these studies suggested it was a fairly uniform disease in most non-A, non-B.

Q. If we just look at the next page, and this relates to the specific patient's group, of those with non-A, non-B hepatitis. Picking it up in the first main paragraph, so the second line on the page:

"Eight haemophilia and 4 nonhaemophiliac patents underwent liver biopsies at between 6 and 36 months after either an episode of acute [non-A, non-B] hepatitis (7) or the first detection of abnormal liver function tests (5)."

Then we can see the results there:

"Four of the haemophiliac patients demonstrated chronic active hepatitis ... and 4 chronic persistent hepatitis ..."

I appreciate the numbers are relatively small, as with all of these biopsy studies, but you have 50% with chronic active hepatitis there:

"Of the 4 nonhaemophiliac patients, 1 had

[chronic active hepatitis] with cirrhosis, 1 [chronic active hepatitis] without cirrhosis ..."

So again 50% of those four with chronic active hepatitis:

"... and 2 had chronic lobular hepatitis."

Just so we don't get confused about terminology is chronic lobular hepatitis to be equated with chronic persistent hepatitis or is it something else?

A. No, it's a third condition. It means that inflammation is distributed throughout the liver lobules. So the whole liver is full of cells. You can't tell acute lobular hepatitis from chronic lobular hepatitis, apart from by knowing the temporal history, in other words how long the patient has had an elevated transaminase, which would indicate that -- if at some stage during that chronic elevation of the transaminases there has been a biopsy, and you see a lobular hepatitis, then that is chronic. If the patient has had abnormal LFTs for, let's say, two or three months and you see a lobular hepatitis, in that time-frame you would say it is probably acute hepatitis, but until you follow that patient, you won't know, because if he goes on to have abnormalities for six months, that lobular hepatitis seen in the first two to three months is presumed to

continue and represents a chronic lobular hepatitis.

So chronic lobular hepatitis isn't that helpful in determining who is going to go on to cirrhosis. It is a group really where you need to integrate their biopsy with the temporal sequence of what has been happening to the liver function tests. Have I explained that all right?

Q. Yes. Thank you. So in relation to this group of eight patients, the biopsies showed 50% of them with chronic active hepatitis; is that correct?

A. Yes, yes, yes.

Q. I think we can see from the next paragraph that of those who were within the haemophiliac group of the eight patients one had received only cryoprecipitate but seven Factor VIII concentrate of a mainly commercial source.

I then want to ask you about two studies that you have referred to in your report to the Penrose Inquiry. I am not going to ask you any detail about the evidence you gave to Penrose. Rather than look at the underlying studies, it's probably quicker just to go to your report and take it from there. So it is PRSE0004640. If we go to page 9, please, this is under a heading of "The changing perception of Severity of [non-A, non-B] hepatitis". Just pick it

up, I think, in the last eight or lines -- I will pick it up with the sentence that begins, about ten lines down:

"Thus in the early days the liver disease was thought to be relatively mild compared to that seen with HBV for instance. This view started to change on the basis of the accumulating data from liver biopsies."

Then there is a reference there to Dame Sheila Sherlock's book which you have already referred to. Then we see two studies there set out. One is a study of which you are a co-author, Bamber, Sherlock, Scheuer and Thomas, 1981, Journal of Clinical Pathology, "Clinical and histological features of a group of patients with sporadic non-A, non-B hepatitis". We have that if we need to look at but I think we can take it from here. You record that study as:

"... showing that biopsies from patients with chronic [non-A, non-B] hepatitis 'covered the whole spectrum of acute and chronic hepatitis and 1 patient had cirrhosis' ..."

Then you referred to a US study entitled "Non-A, non-B post-transfusion hepatitis: disaster after decades?" If we just go over the top, at the

top of the page we can see that is a 1982 publication. You say:

"... also reflected this changing view and pointed out that [non-A, non-B] was a silent and slowly progressive disease which ultimately did result in cirrhosis in a proportion of cases."

Without going to the detail of those two papers, is it fair to say what you were reporting and what was reported in the American publication in 1981 and 1982 respectively is essentially consistent with the message you had given at the symposium in 1980 and, indeed, the work from Sheffield and Professor Preston, published in 1978?

A. Yes, yes. They were all in accord really.

Q. Thank you. We can put that away. Next I am going to ask you just about a handful of the various working groups and committees that you were involved with in the late '70s and early '80s.

The first is the advisory group on testing for the presence of hepatitis B surface antigen. If we could go to CBLA0000931, we can see if we look at the top of the page this is "Note of the 2nd meeting of reconvened advisory group on testing for the presence of hepatitis B surface antigen and its antibody". The meeting is 2nd April 1979. A number of people listed

as present and you are there for Professor Dame Sheila Sherlock?

A. Yes.

Q. Then if we can go to the third page, we just pick up the heading, in the top of the page "Non-A, non-B Hepatitis", we can see there:

"As previously reported the Department was anxious to encourage research directed towards establishing the extent of the problem in the UK and the development of tests for the agent(s) of non-A, non-B hepatitis."

There is reference to the medical research council's interest in relation to that. The next paragraph:

"Dr Dane proposed that clinicians should be reminded of the importance of reporting all cases of post-transfusion hepatitis including those which were hepatitis B negative."

Then there is reference to studies that Professor Zuckerman wants to undertake and then if we look at the penultimate paragraph in this section:

"Dr Vandervelde/Mrs Supran said that the arrangements for the notification of post-transfusion jaundice cases were deficient, as anicteric individuals do develop chronic liver disease and these

cases would be missed using the present system.

"It was thought that there is a need to alert RTDs [so regional transfusion directors] and hospital staff to the possibility of non-A, non-B hepatitis, and urge notification and reporting of suspect cases, sample materials being sent to Professor Zuckerman. Disseminating this information could be via medical journals, eg the BMJ and Lancet. This would be brought to the attention of Regional Transfusion Directors at their next meeting."

It would appear from this, Professor Thomas, that both the Department of Health and the specific attendees at this meeting were particularly concerned by this time, April 1979, about non-A, non-B hepatitis and keen to ensure that there was a proper notification of non-A, non-B hepatitis cases. Is that a correct understanding of what we see here?

A. Yes. Just to briefly re-state it, the only way we could record post-transfusion hepatitis before was jaundice screening, which was really the extreme end. So if the patient went yellow after a blood transfusion, then you knew they had post transfusion hepatitis. But, of course, we know that most cases of non-A, non-B hepatitis are anicteric, they don't cause jaundice, and those cases wouldn't be picked up by

this post-transfusion jaundice screening. Therefore, we were only looking in the public health screening sense at post-transfusion hepatitis with a very insensitive test.

If you used AST or ALT screening -- these are the enzymes, you will recall, that indicate liver damage -- if you look at these after a blood transfusion, as happened in the United States, then you would get many more cases, and this is why -- one of the reasons why we thought there were very few cases in the UK and that the blood in the United States was much more contaminated. It turned out there is a difference but it is not as big as those original data suggested.

Q. Then if we go to just one further meeting of this particular advisory group, it is at CBLA0001020, and we go to the second page and look at the top of the page, this is the third meeting of the reconvened advisory group. The date is 1st November 1979. Again, you are there deputising for Professor Dame Sheila Sherlock. If we could go to the next page, please, Soumik, the bottom half the page, we can see, under the heading "Non-A, Non-B Hepatitis", the first paragraph is an update from Professor Zuckerman about the Medical Research Council Working Party. Then the

second paragraph says this:

"It was agreed that Professor Zuckerman in consultation with Dr Dane and Professor Dame Sheila Sherlock should write to the medical press (eg the Lancet), to draw attention to the possibility of non-A, non-B hepatitis and to ask clinicians to provide serum samples to Blood Transfusion Directors with details of cases of hepatitis occurring after the administration of blood and blood products including Factor VIII, and which had been shown to be [hepatitis B antigen] negative."

Then if we go to the last paragraph there:

"It was agreed that all cases would be notified to the PHLS [so the Public Health Laboratory Service] as well ..."

So, again, it would appear that there's a concern here to enhance medical awareness of non-A, non-B hepatitis and to set in train a system of all cases, not simply those picked up through the identification of jaundice, to the Public Health Laboratory Service; is that correct?

A. That is correct, yes.

Q. Now, you were also lay member of the UKHCDO's Hepatitis Working Party but I am not going to ask you any specific questions relating to your attendance at

those meetings.

Could we next go to a third working party, the Working Party on Post-Transfusion Hepatitis. That's NHBT0000068_049. So we can see if we look at the top of the page:

"Blood transfusion research committee.

"Working Party on Post-Transfusion Hepatitis.

"Minutes of the second meeting held on ... June 25th, 1981 ..."

We can see, again, a number of attendees, including you, again, representing Dame Sheila Sherlock.

If we go to the third page, just picking it up in the third paragraph, it says:

"Dr Howard Thomas said that efforts had been made at the Royal Free Hospital to develop a radioimmunoassay test for non-A, non-B hepatitis using radio labelled convalescent sera from haemophiliacs ..."

Then further details given, and it says:

"Further work was needed with this test."

Can you assist us with what the efforts were that were being made that you were involved with to develop and RIA test for non-A, non-B hepatitis?

A. Yes, I did publish that data. It was from a Chinese

guy who was a research fellow and he was very diligent and what he wanted to do was to try to develop an assay and my laboratory ran all the hepatitis B surface antigen testing and the hepatitis A testing. So after we had done those tests, which were necessary to designate hepatitis as non-A, non-B -- we would have to exclude the serological involvement of those cases -- then we kept that serum for maybe six months or up to two years, depending on how the freezers would accommodate it, and we divided them up into anonymised groups. So there would be one saying "normal laboratory personnel", which was my own and all our staff, one hepatitis B, one hepatitis A, one non-A, non-B, alcohol, fatty liver, autoimmune chronic hepatitis, all the different groups, and renal unit and the haemophilia unit.

If we could develop the test, the only way we could tell whether it might be related to a virus causing non-A, non-B would be by showing that it is more common in the groups where we knew clinically there was a lot of non-A, non-B, which would be the haemophilia unit and the renal unit, but hopefully none in the laboratory staff, including myself.

So what my Chinese research fellow did, he took half a millilitre of serum from one of these specimens

where there had been a transaminase elevation. He prepared an immunoglobulin from it, which is the antibody containing a fraction of blood. Then he used that antibody to coat microtitre wells and then he took another specimen and produced the globulin from it and radio labelled that, in the hope that he would then have what's called a sandwich immunoassay.

He then went to the haemophilia patients. The antibody from one of the specimens was stuck to the microtitre plate. If the serum in that contains the antigen to which that antibody was reactive and then you put on the radio labelled antibody from another patient's residual serum, then you would see a signal, in other words, there will have been binding of the radio label. This he applied to, I think, I don't know, 50 or so from the haemophilia unit, 50 from the renal unit, 50 from my lab staff, 50 alcoholics, in the hope that he might be able to -- he might see a higher prevalence of the antigen in the groups that we knew developed non-A, non-B, and that would be the haemophilia patients. The renal unit also had a high proportion but we hoped not to see it in hepatitis A and hepatitis B or in alcoholics, nor indeed in the laboratory staff populations. This he found, he found that this antigen, which was being detected by these

antibodies, was present in anonymised serum from these various groups.

Then we wrote that up in -- I have forgotten the publication, but you have got it -- which showed that, yes, there was an antigen in the patients from the haemophilia unit and the renal unit but not in alcohol or hepatitis A or hepatitis B cases. We thought "Well, this could be then a component of the non-A, non-B virus", which it turned out it wasn't actually. It was an antiglobulin, but that's why the experiments were done.

The experiments, as I say, were done with serum that was left after we had tested for hepatitis A and B, which was part of the diagnostic service that my laboratory provided in diagnosing non-A, non-B, excluding hepatitis A and hepatitis B. So we kept the residual serum from those cases, which was usually about half to 1 millilitre of serum in the hope they would be of use in the future. We would throw them out after six months when the freezer -- we had two freezers -- when those freezers became full. So that's what that study was about and I think it was Dr Luo -- L-U-O, I think -- of which you have his paper. I alluded to that assay in the Glasgow meeting.

Q. The documents from the early '80s also refer to you

undertaking work with Dr Janossy on diagnostic tests and working with Dr Dane on a radioimmunoassay test for non-A, non-B hepatitis. Are those all separate pieces of work?

A. No. They were all -- because I was developing new assays and trying to find non-A, non-B, I had a collaboration going with Dr Janossy in which we would try to produce most monoclonal antibodies to the components of hepatitis A and hepatitis B, so that we might improve on the existing assays which Abbott produced and which involved sheep antiserum produced by inoculating a sheep with, let's say, hepatitis B surface antigen.

In order to make that reproducible monoclonal antibody technology had been developed by Cesar Milstein. I had shown an interest in that, as had George Janossy, as Professor of Immunology. I purified viral antigens, in particular hepatitis B surface antigen and hepatitis B core. We immunised mice with those antigens and produced monoclonal antibodies, which are pure antibodies. Do you understand? Sorry, I am not being rude but do you understand the monoclonal antibody term?

Q. In fact, one of the questions I have been asked by Core Participants to ask you, which was going to be my

next question, was if you could tell us what you mean by "monoclonal antibodies"?

A. Well, what Mr Milstein showed, with Greg Winters, who was at Imperial, and Alan Fish, if you immunise a mouse with, let's say, hepatitis B surface antigen, then that mouse will produce a heap of antibodies to different parts of the viral protein. So there might be 100 or 200 different antibodies all binding to different parts of the viral antigen. So you immunised a mouse with the antigen and then you took the spleen cells from that immune mouse and fuse them in a myeloma cell, which is a malignant antibody producing cell. Then the progeny from that fusion, so-called hybrids, would have the joint function of or the joint property of being malignant, so they kept on producing the antibody, and each hybrid would produce a different single antibody, because we cloned them out.

So monoclonal antibody is a malignant cell line producing 100% pure antibody to a particular epitope. An epitope is just a part of an antigen. Remember, I just said an antigen might have 100 or more epitopes, fragments of the antigen to which the antibodies bind. Those antibodies are very useful to produce radioimmunoassays or enzyme immunoassays.

I have developed some, with funding from NRDC, I think it was called then, but then it became British Technology Group, and George Janossy and I were funded for a lot of money to produce these antibodies, which would be a leap forward in diagnostic hepatitis testing.

Luckily, we were successful in doing that and we were using that assay, the monoclonal antibody tested assay, as well as the commercial antibody assay for testing four hepatitis B surface antigen. We found that the monoclonal antibody based assay was much more sensitive. We got positives in specimens that were otherwise negative by the commercial AbID assay for hepatitis B surface antigen.

At that stage we wondered whether those extra ones were a sort of spin-off of hepatitis B, which the French and a group in America had suggested, that we were picking up with our monoclonal antibodies and this monoclonal antibody assay for hepatitis B surface antigen might be picking up a non-A, non-B assay. It turned out that wasn't the case, but the assay was subsequently commercialised by a variety of companies, who paid royalties to the Royal Free and a proportion of the royalty to George Janossy and myself and another lady who helped. So that's the basis of that

story.

Q. We can take the document down, thank you.

You say in your witness statement that you offered to provide monoclonal antibodies to Dr McClelland for the purpose of a study. You weren't sure whether that offer was taken up, I think, from what your statement suggests.

A. Right.

Q. What was the purpose of the offer to Dr McClelland?

A. Well, as well as producing antibodies to hepatitis B surface antigen, which is the envelope of hepatitis B, we also produced antibodies to what is called the core, the centre of the hepatitis B virus. We then were able to -- it doesn't matter the detail -- but we produced that monoclonal antibody to produce a very sensitive and reproducible assay to mention antibody to hepatitis B core. Everybody who was infected, either acutely or chronically, and the acute ones that get better, all of this group will have antibodies to hepatitis B core, okay? So it was a good indication of infection, acute or chronic, cured or persistent -- self-cured or persistent -- for hepatitis B.

The Americans and the Germans had used what they call surrogate tests to try and detect high risk donors, high risk donors transmitting non-A, non-B.

They were wanting to do -- the Americans had done this, as did the Germans. They had effectively picked up some cases of non-A, non-B. It was called a surrogate test. Before we had the discovery of the hepatitis C virus, the Americans and the Germans had decided they would use these surrogates, an ALT screen and an anti-core screen to pick up these non-A, non-Bs.

We had a meeting -- I don't know which committee it was -- it was discussion of whether we could use them in the United Kingdom really, and the Blood Transfusion Service were a little bit against it, because they said they would pick up a lot of people, particularly with the ALT part of that combination -- a large number of people with alcohol-related liver disease or type 2 diabetes, fatty liver, which would be true, and therefore before we could determine how useful that ALT screen with the anti-core screen -- and I should add at this stage that anti-core picked up people with a lifestyle which was deemed to be high risks, so a lot of intravenous drug users had antibody to hepatitis B core, as did people with a lot of sexual partners, they might have antibody to core as well.

You probably know that the Blood Transfusion

Service in the UK had been interviewing patients prior to accepting them as donors to try and identify whether they had a high risk lifestyle, for want of a better term. Had they used drugs? Were they promiscuous? So the surrogate of ALT and anti-core was being evaluated and the BTS, Blood Transfusion Service, in the UK thought we were going to get a lot of false positives.

Dr McClelland -- so they wouldn't introduce it on the basis of what had been done in America and Germany. They wanted to see what the yield of infected material by preventing non-A, non-B post-transfusion hepatitis would occur in the UK.

Then the cost of that came up and the Department of -- I think it was Dr Metters, was it, who was the medical officer in the Department of Health at that stage, said "If we did a trial, how much would that cost?" In other words, screening everybody and looking at how many would be taken out. That, when we worked it through, was going to be very expensive. So I said "Well, monoclonal antibodies cost me nothing". I mean, one mouse produces enough antibodies probably for a million tests. So I said he could have that monoclonal antibody assay in Edinburgh if he was willing to do the test.

I gave him the telephone number of Peter Karayiannis, who was an academic colleague in the department, telling -- or asking Brian McClelland to bring him if he wanted to take up that offer, and Peter would have sent him the antibody. But I think for some reason or other it didn't happen.

Q. You said in the statement that your view was that anti-HBc and ALT surrogate, non-A, non-B screening of blood donations should have been introduced. Is that correct?

A. Yes. I thought it was -- we should have introduced it. But at least we should, having heard the counter argument, which we were going to get a lot of false positives -- which was reasonable -- I mean, I took that on board. I thought that it could be reasonable then to do a trial, just to see how many units we lost and whether we did reduce the incidence of post-transfusion non-A, non-B, and then we could work on a much better basis.

That's why -- if we could reduce the cost with free anti-core, which was the expensive component of that trial, then it might make it more plausible -- or possible, rather, not plausible.

Q. Then can I then just turn to the question of screening for hepatitis C once an antibody assay was available?

I am going to direct your attention to an article you wrote with a colleague, Dr Brown. It is NHBT0088770.

This is published in Medical Virology. It is entitled "Blood Transfusion Services Should Have Begun Screening for Hepatitis C When an Antibody assay First Became Available". For, so in favour of that proposition, Dr Brown and you. And then against, Dr Barbara from the Colindale Blood Transfusion Centre.

Then if we can just look at the bottom half of the page, I want to pick up in the left-hand column, three paragraphs up from the bottom it says:

"In the early 1980s it was shown that the incidence of [non-A, non-B hepatitis] could be almost halved by the exclusion of donors with antibodies to hepatitis B core ... or abnormal liver function tests ..."

I think that was the issue you were addressing a few minutes ago. Then:

"The presence of these surrogate markers for [non-A, non-B] hepatitis resulted in a loss of only 4% of the donors."

Then you refer to the identification in 1989 of the hepatitis C virus.

Then you say at the bottom of the page:

"In this paper, the argument for 'Blood transfusion services should have begun screening for hepatitis C when an" -- if we go to the top of the next column -- "antibody assay first became available' will be developed by examining what is known about the serology of hepatitis C to determine (i) how many donations would be excluded by screening for anti-C100, (ii) how many cases of [post-transfusion hepatitis] could be avoided by eliminating blood products positive for anti-C100 and (iii) how many cases of [post-transfusion hepatitis] would not be prevented by such a screening programme."

I am not going to go through the detail of the arguments, but we just pick up your conclusion, bottom of the next page. Under the heading "Conclusion", very bottom of the page:

"The introduction of an HCV screening programme for blood products using the anti-C100 assay would cost about £6-25 million/year, would result in the loss of", top of the next page, "12,500 to 25,000 donations/year and prevent between 2,500 and 5,000 cases of [post-transfusion hepatitis] per year. Between 1,250 and 2,500 cases of chronic liver disease ... [per] year and 250-500 cases of cirrhosis/year could be prevented, but a similar number of cases

would still occur because of the 50% sensitivity of the test."

Then you go on to say:

"Patients with CLD [chronic liver disease] will consume NHS resources as they develop the complications of portal hypertension; the cost of 250 liver transplants is about £8.75 million. It would seem to us therefore that there are financial as well as ethical considerations in HCV screening. Clinicians tend to underestimate the magnitude of the problem as 75% of PTH cases are anicteric; if we are not doing everything possible to prevent NANB PTH we may find ourselves in a difficult situation when the first group of cirrhotics in the anti-C100 era become litigious."

Then we have Dr Barbara's counter argument in the rest of the article.

I think you said in your statement, Professor Thomas, you don't have really anything to add to that, but it is a perspective that we have not yet explored and I wanted to ask, in addition to publishing this article, whether you were involved in any meetings or discussions with the Department of Health or Blood Transfusion Service as to whether this screening should have been introduced?

A. Well, it was my view that we should introduce it. I should say in the context of this article that I guess -- the editor of this journal was Professor Paul Griffiths, who was the Professor of Virology at the Royal Free, and he had just set up this journal and he was looking for someone to write in favour of this, as opposed to a member of the Blood Transfusion Service, whom he knew would be able to write against it.

It was almost -- as I think I said at the Penrose Inquiry, this was the sort of adversarial format -- or, not an adversarial format but a -- where -- a bit like barristers, you know. One would present one case, one aspect of an argument, I suppose the defence, and another would produce the defence (sic), you know. So I -- because I was a physician, and physicians in the main are interested in individual patients, whereas the Blood Transfusion Service and epidemiologists are much more concerned with populations of patients and economic issues.

So I thought it would be useful for Jonathan Brown to work this through -- he was a registrar in my department -- so I asked him to do this. We sat down and talked about how we might do it and that's how it came about.

I can't -- I mean, there was this discussion, not only about ALT and anti-core screening, as I alluded to, which was in the context of blood transfusion, but there were discussions also on -- which I think I was present at -- you know, looking at whether we should go with the stage 1 or the first available assay of anti-core or whether we should wait for the second format, which was likely to be ready in a year and would get rid of a lot of the false positives.

So in answer to your question, this is how I felt about it. I thought it would be useful to work it through economically, because that would give solid facts, but there is an ethical issue as well, and Dr Barbara genuinely thought they would be losing large numbers of units of blood and they wouldn't be able to supply enough blood because of all the false positive blood that would be lost. I could see that argument as well. We were both friends and would we said, "Well, let's do the best and write the arguments for and against", and that's what we did.

I mean, it must have been taken up subsequently, but I didn't hear any more about it, you know, as to whether it had been introduced or not at the time until it came through and it turned out it

hadn't been introduced and that we were going to wait until, I think, 1991, September, for the second generation assay, which had got rid of a lot of the false positives, which was more acceptable to the Blood Transfusion Service because they would lose a smaller number of units of blood.

And, you know, it's a proper concern, isn't it? That, you know, if you are involved in a blood traffic accident or you are going to have cardiac surgery, you will expect the Blood Transfusion Service to provide enough blood for you to get through that quite safely. So he presented the argument for that and I presented the argument for the number of patients who might die by not using the first generation assay. So that's the situation.

Clearly then it went internal into the health service and -- into the health service and someone somewhere decided that they wouldn't introduce it.

Q. The next and, for present purposes at least, the last lot of questions I have for you, Professor Thomas, relate to a study which Dr Kernoff was involved with and in which you were involved.

If I can pick it up in your witness statement at WITN3824007, and if we can go to -- can we try page 10, Soumik. Mine is in a slightly different

format. Yes.

So if we pick it up at the top of the page, you refer there to a:

"... prospective study of 30 patients recording the incidence of abnormal LFTs and persistent abnormalities after infusion of cryoprecipitate, NHS factor VIII And IX or USA factor VIII concentrate ..."

Then you refer in brackets to the article itself:

"... (High risk of [non-A, non-B] after first exposure to volunteer or commercial Factor VIII ...)."

We will look at that in a moment.

Then you say:

"This was done because abnormal liver tests had already been reported in USA and it was important to know in each case whether the abnormality had been there before treatment in which case it would not be due to [post transfusion non-A, non-B] hepatitis ..."

You refer a little further down to the study being:

"... supervised by the Haemophilia Unit and Professor Kernoff states in the paper that the study was approved by the RFH Ethics Committee and all patients gave verbal consent."

You say your contribution, as a hepatologist,

was to provide advice on management of the liver abnormalities.

I am going to ask you to look at the paper. I have some questions I have been asked to ask you. I don't know whether you are going to be able to assist with casting further light on this but you will appreciate they are not questions I can pose to Dr Kernoff.

So if we go to PRSE0003439.

So this is the paper you have referred to in your witness statement:

"High risk of non-A, non-B hepatitis after a first exposure to volunteer or commercial clotting factor concentrates ..."

And then we can see the authors there: Kernoff, Lee, Karayiannis and you.

Then we see the summary:

"After a first exposure to factor VIII concentrates, 9 [out of] 9 British patients treated with USA-derived commercial products, and 10 [out of] 12 treated with British volunteer (NHS) products, developed acute non-A, non-B ... hepatitis. Hepatitis following commercial products was more severe, and of shorter incubation."

Et cetera.

Are you -- I don't know whether, as I say, you can assist with this, but if, as your witness statement suggests, this study was undertaken because of concern over reports of abnormal liver function tests from the USA, what was the justification for Royal Free Hospital patients being moved from cryoprecipitate to factor concentrates?

A. Well, I think the context of this was that -- I mean, all the patients that went into this study had come into the haemophilia unit at the Royal Free either with a bleeding episode or, latterly -- I am not sure whether the second group I am going to mention were involved here, but -- or, latterly, when Factor VIII concentrates were used prophylactically. In other words, the haemophilia population found, you know, the concentrates very patient-friendly, if I can put it, to a patient, but, you know -- because we didn't know about any of the problems that were being transmitted. But, you know, if you had a painful haemarthrosis, bleeding into your joint, which your doctors would tell you would cause fibrosis and deformities, then an injection of this material stopped that. And very soon after it was a natural extension of this to ask, "Well, if we took this three times a week, would it prevent having haemarthrosis and muscle bleeds and

things?" So these young, in the main, boys, in the first few years of life, could then actually play and develop normally as normal children.

So the use of these concentrates at this stage was very important. People wanted to have them. I think what shouldn't have happened, and the haemophilia directors, of which Peter Kernoff was one, had argued that only if you had severe haemophilia, with virtually -- I am not a haemophilia doctor -- virtually a total deficiency of the Factor VIII in your blood, would you need these concentrates. If you had mild haemophilia, you could be treated with cryoprecipitate, which was derived just from eight units of blood. And already it was known that the risk of getting non-A, non-B hepatitis after cryoprecipitate use was much less than if you used concentrates. And there was an agreement with the haemophilia directors that -- you know, what the cut-off would be, which patients would get vasopressin, which released any remaining Factor VIII globulins from the patient's liver cells, or could be treated with cryoprecipitate rather than the higher risk concentrates.

Of the group who had the more severe haemophilia, when they came in with a bleeding

episode, they would be -- in the middle of the night often -- they would be given concentrate. And I think what Peter Kernoff decided to do, with the agreement of the ethics committee and the consent of the patients, randomly allocate them to whether they received NHS or commercial material. And they were also following transaminases at this time, to see whether, you know, patients did get ALT abnormalities, and essentially virtually 100%, whether it was an NHS concentrate or commercial concentrate, got abnormalities.

That was predictable in a way, because the incidence of hepatitis non-A, non-B was something like 0.5% in human -- in British donors and about 2 or 3% in American commercial donors. And since something like 1,500 litres or donations of blood were used for each preparation, every single preparation would be expected to contain the virus. And indeed this is what turned out to be the case.

So what this study showed, in patients who should have all had severe Factor VIII deficiency -- and I don't know whether any of them -- are there any in the list of patients who had mild disease? Because if there were, then those people shouldn't have had the concentrates. They should have had the

cryoprecipitate.

I think the intention was it should only have been those patients who could only be treated with the concentrate who would have been included in this study. I think the protocol would have said, I presume, that anybody with mild disease should not be included, because they should be getting cryoprecipitate, and indeed the majority would have been. So I think that's the background to it.

Afterwards, when it turned out -- Professor Kernoff found that virtually everybody developed abnormal transaminases after the use of these concentrates, he then wanted to ask the question of: was there an antibody out there in people who had had concentrates in the past and had normal transaminases, indicating that they possibly had recovered from a non-A, non-B infection? If you used the globulin from their blood, an antibody containing globulin and gave it with the concentrates, where he knew there would be 100% incidence of non-A, non-B, if you give this antibody, could you prevent it happening?

And again, he explained that to the patients, and there was I think one or two cases where it looks as if the immune serum globulin, as it was called,

prevented Factor IX deficient patients, receiving Factor IX concentrates, from developing hepatitis. But it was -- it's one patient, it says here, just one patient prepared to be protected. Which wouldn't seem to be significant but did suggest that there might be something called protective immunity which might be useful in this context: severe haemophiliacs receiving concentrates where they are all getting ALT abnormalities.

I think that's the background of it, in the main.

Q. You said, Professor Thomas, that Dr Kernoff discussed matters with the patients and consent was given. Do you have any first-hand knowledge yourself of what was said to the patients who were participating in this study?

A. No, but -- I mean, Peter Kernoff was an obsessive individual. I mean, he ran the unit with a rod of iron. And the reason occasional patients may have got concentrate when they should have had cryo, if it was mild haemophiliacs, was related to the fact he would set up the rules and the patients who came in in the middle of the night would be looked after by a registrar or a haemophilia nurse, who would be, in the middle of the night, looking for a concentrate in

a freezer. And the only thing that Peter tried to do was make sure that any one patient, if they had repeated episodes of either bleeding or having the Factor VIII concentrate prophylactically, in other words to try to prevent bleeding episodes, that that patient's material was all kept aside from one manufacturer, whether it was British or American, so that they all got the same -- that that individual would always get the same batch, which would, he thought, reduce, if anything, the chance of them being infected.

So Peter organised it extremely well. And Christine Lee took over as the head of the unit, technical unit. Professor Ted Tuddenham mainly did research but Christine, I think, was the head of the clinical service, and I think you have interviewed her, really.

My role came in when -- if they had developed abnormal transaminases, what it might be due to. And that is when, you know, there was a discussion as to what we should do, because we had done a trial in patients with non-A, non-B outside the haemophilia population and showed that interferon normalised their liver test abnormalities. We wanted to discuss, in the context of their liver, a joint clinic, where we

had a registrar from the liver unit and a registrar from the haemophilia unit, plus or minus consultants in both those units, seeing all the cases in the haemophilia unit that had abnormal liver tests. And at these clinics that's where there would have been discussions on behalf of the liver unit as to what might be done. And we decided we would try to -- having published in the BMJ the demonstration that liver tests became normal in non-haemophiliac patients with non-A, non-B when treated with interferon, that we would try it in the haemophiliac population.

It was a separate issue, because, of course, because of the bleeding problems with a haemophiliac, we would have to give it probably not intramuscularly but intravenously and with cover of a coagulation factor, which would involve giving more of one of the concentrates.

Which is why I know that Peter Kernoff would be very keen to make sure that there would be a batch from one manufacturer which had a patient's name on it, which would only be kept for that patient, for instance, so they always got the same material. That was one of the things he was concerned about if we went into this trial, would be: since they would have to get concentrates, which his study had shown were

transmitting non-A, non-B, he wanted to make sure that he wasn't giving them a second episode, because we thought there may be two viruses at that stage. So he used the same batch.

Q. As a --

A. So that was the background to all of that. And the trial was successful in the non-haemophiliac patients and that was published in the British Medical Journal.

Q. Just sticking with the study that we see here, as a hepatologist involved with this study, was it your expectation that the patients who were being enrolled in it and participating in it should have been advised of the risks of developing non-A, non-B hepatitis from the factor concentrates with which they were going to be treated?

A. Yes. I mean, these patients were drawn from the haemophilia clinics, and I think Peter and Christine say that they were asked for informed consent and the ethics committee of the Royal Free were asked to comment on it. Does it not say that in that text?

Q. It says they were asked to give consent but doesn't provide full details of what that consent process would have entailed.

So my question to you is, as a matter of principle, would you expect the information given to

patients who were being asked to participate in the study to have included an explanation of the high probability, if not near certainty, of developing non-A, non-B hepatitis?

A. Yes, I think you would have had to, you know, say there are two preparations and -- you know, "You would need to have one. We don't know which is the better one", although you might argue I suppose, you know, there was a suspicion, although it turned out to be wrong, that the American one was going to be more of a problem.

But I think it is worthwhile saying here that although -- because of the background information that was around, which was -- I think there was a paper from Oliver James, for instance, showing that after cardiac surgery -- in Newcastle -- the incidence of non-A, non-B after use of British blood was very low, whereas after cardiac surgery in the United States it was very high. But there was a feeling that even if it was low, as in the Newcastle study -- I think he said it was about 0.2% -- each patient for cardiac work would have about 6 or 8 units of blood. So the total risk would be about 1.5% of getting ALT elevation after transfusion, whereas the American incidence was two or three times that.

But we weren't -- the concentrates were being made from 1,500 units of blood. So even accepting the very low incidence of infected blood in the UK, on the basis of the Newcastle Oliver James study, every pint, every unit of Factor VIII concentrate would contain the virus. And indeed that turned out to be the case.

So I think they had reason to believe that hepatitis C was going to be the same after a volunteer, UK or American, but what was not going to be the same was the HIV incidence, because patients had not yet been described, as far as I can recall, in the UK, whereas in California and in the America system, HIV had already been described.

So there was going to be, I thought anyway, no difference in the prevalence of hepatitis C, non-A, non-B, with these two concentrates, but HIV, I think, probably with the benefit of hindsight, might have been shown to be different, because they had already seen it in the US and we were still looking for it in the UK.

That is quite a complicated issue really, and ...

Q. Yes. I am not going to be asking you about HIV.

Just two further questions in relation to this study. Do you recall how soon after the commencement

of the study you began to receive abnormal liver function test results?

A. You mean after this --

Q. In the course of this study --

A. Yes.

Q. -- how soon after the study commenced were abnormal liver function test results being reported to you? Are you able to recall?

A. I can't recall really, because, as I say, I was involved, you know, in looking at how we would manage these patients afterwards and what the significance would be and also what we would need to do to find out what the cause of the abnormal ALT was, because at that stage there were at least three hypotheses. One was that it was a virus; the second was that it was due to chemicals which are used in the preparation of the concentrates, preservatives and what have you; and the third was that it might be related to immunisation against HLA proteins, human leukocyte or transplantation antigens, which can cause immunosuppression, which was relevant because the other thing that was of concern was whether HIV was being seen in British patients at that stage, and I think there were a lot of reasons why the patients with haemophilia might be immunosuppressed, one of

which was just there was a lot of materials other than Factor VIII in the concentrates. HLA proteins, beta-2 microglobulin were two which could depress the immune system.

So my contribution was to think of a better test which we would apply to each person when their ALT was known or perceived to be abnormal, to find out what it might be. It might have been due to hepatitis B, for instance, because there were some concentrates which were transmitting hepatitis B, for instance.

Q. As it became -- sorry.

A. So that was my role, to look at what was happening and why the patients had got abnormal ALTs.

Q. As it became apparent that the patients enrolled in this study were developing post transfusion non-A, non-B hepatitis, was it, in your view, ethical to continue with the study?

A. Well, luckily I wasn't involved in that situation. I suppose if they were seeing an equal incidence of abnormal transaminase in both groups, then I don't know -- was this -- I have forgotten now. Was this blinded; in other words, did they know which group were getting which product?

Q. I am afraid I don't know without checking, professor,

whether that's the case or not.

A. But I think they must have -- bearing in mind the prevalence -- the incidence, rather, of abnormal liver test was the same with all the concentrates, they must have seen abnormal LFTs in all of the patients, you know, in the follow-up, and -- in which case, if you are seeing it after, you know, both and you are giving it for a bleeding episode, you know, you must know it is ethical to continue.

You know, the patient must get something. Or are you suggesting they might have at that stage switched to cryoprecipitate?

Q. That's the inference, professor, yes, not least because these are patients who were being exposed to concentrates for the first time, as the study tells us.

A. Oh, right. Yes.

SIR BRIAN LANGSTAFF: I was just going to ask about that. These were all patients who, by definition presumably, to be entered into the study, had no obvious sign of suffering from non-A, non-B hepatitis?

A. Well, presumably. Did they have ALTs beforehand? I think they did.

SIR BRIAN LANGSTAFF: Well, if they did and they were entered knowing that they were suffering from

hepatitis, that's one thing, but in that case one wonders why the study was going to be of any value.

A. Well, it wouldn't have been of value. Had they had abnormal ALTs before, then you wouldn't have been able to determine anything.

SIR BRIAN LANGSTAFF: The object of the study is to take people who had not shown any signs of non-A, non-B hepatitis and administer to them a product which it was hypothesised might give them less hepatitis if it was NHS-made and give them a lot more risk of it if it was commercial, on the basis that probably one or the other would provide it. There would have to be some therapeutic reason for the treatment.

How was that anticipated -- can you help -- in advance of the study actually being conducted that they were people who, although they have never had concentrate before, were likely to or might need it in the future, so that they could then be studied and asked for their consent to have this product administered to them?

A. Well, surely, the -- I mean, what -- I have not gone back over this recently and I assumed you would ask Professor Lee about this. You know, if somebody comes in -- these were severe haemophiliacs, I think, where vasopressin, which releases the patient's own

Factor VIII or cryoprecipitate, were ruled out. So the protocol I presume would have said patients coming in with bleeding episodes in the middle of the night or during the day would need treatment with one of the concentrates. So, you know, they would give one or other of the concentrates to treat the episode.

SIR BRIAN LANGSTAFF: I think rather than speculate -- I have read the study at least a couple of times, but I probably ought to re-read it because it will answer the question I just raised.

MS RICHARDS: Yes. Sir, I was just going to point out, some of the patients, a minority, were "virgin haemophiliacs", that awful phrase, and most were described as needing infrequent treatment and therefore, I think, would be unlikely to be severe haemophiliacs. That's the bottom of page 2 of the report.

SIR BRIAN LANGSTAFF: Or severe haemophiliacs who just happened to be in that rare group that would require very little treatment.

MS RICHARDS: Yes.

A. Well, I think -- you know, obviously you can't interview Peter Kernoff, but the haemophilia doctors who were taking care of these patients at this time you can ask about these issues. As I said, my role

was to work out why they had abnormal liver function tests after these concentrates, and you might say "Well, surely it would be obvious?", but, as I say -- and I think in other studies that were published at this time, some patients had hepatitis B and C at the same time. Some had hepatitis B and had delta virus infection as well, and there were other patients who had other, you know, problems. So, you know, we were trying to, at that stage, also look at patients who had persistent abnormalities to see whether or not they should have -- whether they needed a liver biopsy to determine this issue of whether they had chronic persistent or chronic active hepatitis. In the main, I think this was after we had already determined that they had not had chronic active hepatitis, so I don't think any of these did have liver biopsies. But you really need to ask the haemophilia unit what was going on. I saw them afterwards, after it had happened. But that's all I can say about that at the moment, unless you want me to read it again, because I --

SIR BRIAN LANGSTAFF: No, no. I think you have answered very fairly in saying that, in essence, the study was one which was organised by the haemophilia unit, and we have already asked Professor Lee about this general area and about her study. So I think I don't trouble

you any further.

MS RICHARDS: Sir, those are the questions I have for Professor Thomas.

We obviously need to give an opportunity to Core Participants and their legal representatives to suggest any further questions arising out of Professor Thomas' evidence today. So if we could take a break at this stage to enable me to receive and consider any questions, and obviously to give Professor Thomas a break as well.

SIR BRIAN LANGSTAFF: Yes, absolutely.

Just by way of explanation, professor, there are quite a number of people who plainly aren't here at the moment -- they are also remote -- who are watching, who are entitled to ask, through counsel, questions which they have in their minds arising out of what you can say.

Counsel will receive and field those questions and ask those that are appropriate to you when we come back, which will be at 4.10.

A. Okay. Thank you very much.

(3.36 pm)

(Short break)

(4.10 pm)

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: Professor Thomas, I have some various questions, so we will dot around from topic to topic because they have been identified --

A. Could I just ask, in fairness to Professor Kernoff, who is dead, I have just read that paper during the break, British Journal of Haematology, I just wanted to make one other comment, really. Is it possible to show that again just so that people can see precisely what I am talking about?

Q. It is PRSE0003439.

A. If we go to the "Patients and methods" section.

Q. Page 2.

A. It is the third paragraph down. It is on page 471.

Q. Next page, please, Soumik.

A. Next page, please.

Q. Did you say it was the third paragraph, professor?

A. On that page it is the second paragraph down, and particularly here:

"Treatment was given either ..."

I just wanted to paint the picture really:

"Treatment was given either to stop bleeding or as prophylaxis before surgery. Duration and dosage of therapy, and choice of therapeutic product, were influenced by clinical circumstances, local availability of products, and departmental policies

which operated at the time treatment was given. These policies changed over the period of the study ..."

Just to make clear these patients were actively bleeding or were just about to go into surgery when it was known they were bleeding. These concentrates were not given electively, if you like. They were given as a method of treatment or, in the case of the surgery, obviously, in the anticipation that there would be bleeding. So they had to give exactly what was available. Then they determined what each patient had had after the event.

The reason they did serial LFTs afterwards was what we alluded to before and that was that just looking for jaundice after an episode of treatment would miss a large number of cases. We already knew that post-transfusion hepatitis was occurring after use of concentrates and after single units of blood on occasion. It was important to know, in individual patients, for their own clinical care, whether they were one that was getting these problems. So the context was an acute bleeding episode, or before surgery, in the context of knowing that liver function tests were occurring, abnormalities were occurring after use of these concentrates, and they wanted to regard whether each individual patient had this for

research reasons to see what the frequency would be, but also in terms of management of the patient, because there were lots of causes of abnormal AST, as I mentioned non-A, non-B being the main one but some people had hepatitis B and there were other causes, chemical toxicity in the liver.

So I just wanted to make those points really, because if Professor Kernoff were here I think he would point out that, in the context of a bleeding episode, mistakes are made and I think there were one or two -- at least one case I know of -- where it probably would have been, if it was decided in a cool, calm, collected way that the patient received cryo rather than concentrate, but he does say it is dependent on what's available really.

So that's all I wanted to say, really. No doubt, as I have said before, you have had a chance to talk to Dr Lee about this (over talking).

SIR BRIAN LANGSTAFF: I think one of our difficulties may have been that Dr Lee may have taken up her post when the study was well advanced and a prospective study -- if patients are enrolled in a prospective study at the start, one would expect the patients to be told then what they might expect later. So it was really the issue of consent that inspired the questions I asked.

I have to leave it there, because Dr Kernoff would have been person to ask and, of course, we can't.

A. Yes, yes, but I would just say, as I did say, that he was a meticulous person and he has written in the paper that the patients were appraised of what was happening, although I notice some of them were three or four months of age, so it would have been parents that they were talking to. Anyway that's all I wanted to say on that. As I say, the haemophilia doctors are the ones who would be able to give you more information, although I don't want -- I was involved with the study and I was involved in the discussion afterwards. So I don't want to argue that I wasn't involved; I was. I was involved in what the cause of the LFT might be.

MS RICHARDS: Sir, unless you think it useful, I am not proposing to ask Professor Thomas further but I have no doubt we will receive submissions about this study in due course from Core Participants.

Professor Thomas, in your statement you say -- and this is -- if I just put your statement up on screen, it is WITN3842007 -- you are ahead of me. If we go to page 6, paragraph 12, you say:

"Hepatitis after blood transfusion was quite

common (2-3%) in the UK and perhaps 10% in USA."

Are you able to assist with what the basis is for the figures you have given there in relation to the UK?

A. I think the best study was the one I alluded to just before the break and that was there was a study of cardiac surgery patients in Newcastle. The senior author in that was Professor Oliver James. So if you put into NIH PubMed "Oliver James", I think this should come up. He calculated that, I think -- he said that on average people after cardiac surgery received about six or seven units of blood and after an individual unit, I think he thought it was about 0.2 or 0.3, something like that, of each unit of blood was calculated. Of course, the calculation was the other way round. I think he found about 2 or 3% had abnormal LFTs after cardiac surgery. On average, they had had six units of blood. So he computed that the number of infected units was 2 or 2.5 divided by 6, which would give a figure of about 0.6%.

So it is worthwhile pointing out, this is the hepatitis after blood transfusion. The number of infected units would be dependent on the number of units that we used in each transfusion. He calculated that to be about six. So if you want the incidence

per unit of blood, it would be one-sixth of between 2 and 3.

Q. No, no. I was just trying to understand --

A. Sorry. The US study was the basis -- there was an NIH study, National Institute of Health study at Bethesda where I think that was -- well, Jay Hoofnagle was involved and they were looking prospectively at doing ALT screens after blood transfusion, the percentage that were abnormal, and I think it was around about 10%. The other name to pick up is Blaine Hollinger from Texas. He also did a post-transfusion hepatitis incidence study.

Q. We can take that down. Thank you. The next question I am asked to ask you relates to stage 1 Skipton decisions, intravenous drug use. How would you have dealt with a case where there was evidence to suggest that there was a route of transmission through transfusion of hepatitis C, prior to evidence of intravenous drug use, and then evidence of intravenous drug use post transfusion? Is it the case that the record of intravenous drug use would still have been enough to lead to the claim being rejected?

A. I think if you could be sure that the hepatitis was noted before drug use, then, of course, you could say that it was due to the blood transfusion, but how you

know when an individual starts using drugs is more difficult to determine really. Since it is addictive behaviour, people aren't making open choices really -- they are addicted -- it is difficult to know when the various things started. But if it was, you know, validated -- demonstrated incontrovertibly that the blood transfusion occurred and there were abnormal LFTs and the drug use started later, then, yes, that should have been adequate.

Q. Was there ever in relation to Skipton decisions, whether stage 1 or stage 2, a policy of deliberately delaying or deferring decisions in borderline cases to see if the virus would progress or clear?

A. No, I certainly didn't know of any instances of that really. Whether it was an acute episode -- 20 or 30% would have cleared -- or whether it was an established chronic episode, where 1% might clear after six months, you know, we never waited or -- we just took it at face value and looked at the statistical probability, but the former was much more common than the latter.

Q. Still with stage 1 Skipton applications, I want to ask you about this hypothetical scenario. If you had an applicant who was known to have had a particular operation, if there was evidence of, say, 10 or 20% of

patients for that kind of operation needing a transfusion and the applicant's recollection was that they had a transfusion and there was no evidence of any other risk behaviour, so no evidence of IVDU, or anything of the kind, on what basis could it be said that the claimed blood transfusion was not the probable cause?

A. If I, as I was, the first person to look at this, and I estimated it to be 20% probable, I would probably have to turn it down, but if I was on the appeal committee, I would have let it through. What I am trying to say the process we had was that where there was subjectivity, it should be applied at the appeal committee stage and we should stick, as best we could, to hard facts in determining, you know, what should be the right way forward for the first step of the evaluation.

Q. Did you feel an obligation to the Department of Health or to the NHS more generally to limit stage 1 and stage 2 approvals or take a more purist objective approach, given what you described in your earlier evidence as large amounts of NHS money having already been spent?

A. Well, as a scientist I wanted to do what was right. I mean, I came into this as a volunteer after I was

Chairman of the advisory group on hepatitis and I was asked whether I would like to help with this and I said "Yes", but I am also a clinician and I recognise that throughout my career there have been major constraints on healthcare and funding of it, but I was not at all negative at the starting point over whether a person should get it and, indeed, in fairness to the NHS and the Department of Health, we were never limited on the number of cases that we could fund, you know. If they met the criteria and greater than 50% probability was NHS, at stage 2 nobody ever said -- you know, we could recommend unlimited numbers for this.

So that's the situation I took but, as a director of the Skipton, of course, we did get serial, you know -- at each yearly, Annual General Meeting of the Board of Directors we were given figures as to how much had been given out and these sort of things. So whether it has a subconscious effect, I don't know, but we didn't consciously go in to try to limit the spend.

Q. In relation to stage 2 assessments, if you had a form from the applicant's own clinician setting out their view that the patient was cirrhotic, why was there ever a need to look behind that, rather than Trust the

doctor most familiar with the patient's own diagnosis?

A. Well, I mean, it is partly dependent on whether -- on some occasions, it would be a general physician who, although he might be a very competent and expert general physician, he wouldn't be an expert hepatologist. So, you know, one looked at the basis for why that individual had come to the conclusion that it was a stage 2 triggering stage that the patient had reached, you know, and, just as you have asked me whether I came in with any sort of baggage, for want of a better phrase, you know, of whether I wanted to save money for the NHS, I think most of the physicians filling in these forms really genuinely wanted to look after the interests of their patients and they would be a bit like defending counsel, really.

They would want to, you know, present the best case that they could. We were in a different position. We were in the position of having to evaluate it, depending on the data that was on the sheet, not in terms of the person's opinion.

Q. The next question is about natural clearers. To what extent has the updated medical knowledge about the effects of hepatitis C, which has come to light over the years since the Skipton Fund was first set up,

suggest there should be a reassessment of the exclusion of natural clearers from the schemes?

A. It was known right from the earliest days, back in 1989/1990, that 20% or so of people cleared the virus, as determined by clearing hepatitis C RNA measured by PCR, and then they were just left with antibody. You know, if you found somebody with antibody but who were RNA negative, the probability was, since after chronicity only a very small number would clear the virus leaving antibody, hence the 1%, statistically it was much more probable that it was an acute clearing in the first three to six months, rather than a chronic, longer than six months of infection, clearing in the later stages.

The latter would have, under the rules that were mandated by the Department of Health -- well, the former wouldn't actually have qualified by the rules.

Q. Is it your view that the position in relation to natural clearers has not changed?

A. I don't think it did. We had, you know, RNA, so-called NAT acid -- nucleic acid tests for the virus, direct measure of the presence of the virus, and antibody tests right the way through from 1991 to the present time. That study that I mentioned in NIH, they were able to do sequential studies looking at,

you know, whether there was a window period when there was RNA right at the beginning but no antibody, and then the transaminase rise indicating liver damage and then a period when the RNA would disappear and the antibody would appear.

So, you know, that natural history of the serology was evident in the 1991/92 period and is the same present today.

Q. You told us about your research as regards the link between hepatitis C infection and damage to the brain and, indeed, we have got the papers in materials to which you have referred. Are you able to assist with this: to what extent does that damage to the brain have an impact on the functioning of the whole body and not just on cognitive functioning?

A. Well, we were able to say the virus was in the brain because we had done this spectroscopy of the brain and we found the same pattern in hepatitis C as we had found in HIV, which had previously been known to infect the brain, and, in addition, there was a brain bank in Edinburgh and they will give pieces of post mortem tissue to you if you want to look for various things. We were able to show the virus in the brain from those tissues and the virus that we cloned from the brain was different from the one that we got from

the same individual's spleen or liver.

So, you know, that showed that in some cases it was in the brain but, in any individual before the patient -- if they die, before we get post mortem material, we couldn't say whether the virus was just in the blood or whether it was in the blood and liver and, in addition, in the brain.

But, I mean, do you think the question is related to the fact that the brain might -- if there was a dysfunction of the brain could it cause blood pressure changes or things like that? Is that what you are thinking about?

Q. Well, it is a question I have been asked to ask, so I have no greater insight than the question I formulated.

Damage to the brain may have an impact upon cognitive functioning. I don't know whether you can answer this or not. Does the damage to the brain that you identified have any wider impact upon the functioning of the body?

A. Not that we are able to demonstrate.

Q. The next two questions, I think, relate to hepatitis B. As part of your work over the years on hepatitis B, did you come to any conclusion about the efficacy of the screening for hepatitis B that had

been introduced in the early 1970s?

A. In the general population or in the haemophiliac population?

Q. I am afraid I am simply asking a question as articulated to me. So ...

A. Well, perhaps let's interpret in as in the context of infected blood. I mean, all blood was screened for hepatitis B surface antigen from -- I don't know -- the discovery of hepatitis B, certainly in the 1960s, and those sensitive assays that were available at that time were immunoassays, whether it was radio or enzyme assays, and that really removed most of the hepatitis B-related post-transfusion hepatitis, you know. It was fairly prevalent in the 1940s, 1950s wartime period, but post the discovery of hepatitis B and the availability of radioimmunoassays against hepatitis B surface antigen, it was pretty much dealt with.

Then just to finish, they went into NAT assays, nucleic acid test assays where they look for hepatitis B virus DNA, in the way that I have just been describing, you can look for hepatitis C RNA. Then there is virtually no hepatitis B post-transfusion.

Q. I think that does answer the question, thank you. Did you yourself participate in any research to establish

the prevalence of hepatitis B infection amongst haemophiliacs?

A. No. I think there was quite a bit from previous periods, you know, the older haemophiliacs. The other problem about determining prevalence was what we call passive transfer. So cryoprecipitate and concentrates contain antibody, particularly the cryo, because it was cryoprecipitate of blood, and we were passively transferring antibody to surface antigen or antibody to core. That meant you couldn't tell whether they had had an active infection or if it was this passive transfer of antibody which was causing the positive in the antibody assays.

Reading between the lines, you know, without having solid data, I think there was a lot of hepatitis B in the haemophiliac population from earlier periods before the screen (inaudible).

Q. We have explored, I think to some extent, through the mechanism of the Kernoff paper, hepatitis C prevalence in commercial concentrates versus NHS concentrates. What about the position in relation to hepatitis B? Do you have any knowledge or understanding of prevalence of hepatitis B in commercial concentrates as opposed to NHS concentrates?

A. No, not in a comparative sense, but some concentrates

did transmit B as well as C. We wrote one such case up. Another concentrate transmitted hepatitis B plus delta and C. So there was all sorts of -- carrier for all sorts of viruses in that concentrate, many of which we probably don't know about today.

Q. Then the last question reverts to the Skipton decision-making, in particular, I think, in relation to stage 1. You referred to being a scientist and you have used, from time to time, I think, language of being sure and not wanting to undertake a subjective assessment, which you left for the Appeal Panel, wanting to undertake a more objective assessment.

Do you think it is possible you may have been applying a scientific standard higher than balance of probabilities?

A. I doubt it actually, because the 50% probability was difficult enough to achieve in the absence of, you know, case notes. So we were really pushing the boat in favour of passing those. I'm thinking about the times when we went to look for scars -- the patient provided a picture of scars which might indicate they had an operation where there was a probability that the majority of patients having that operation had a blood transfusion. So, no, I don't think I am being too stringent with it.

Although I claim to be a clinical scientist, I spent every day of my life seeing patients. So I prefer to be known as a clinician and a scientist.

MS RICHARDS: Sir, those are the additional questions that I am proposing to ask.

Questions by SIR BRIAN LANGSTAFF

SIR BRIAN LANGSTAFF: Just one area that I would like to explore with you, if I may, and benefit from your knowledge at the time.

As I understand it, post war -- or during the war and immediately post war, as you have already told us, hepatitis was a well-known risk of transfusion.

A. Yes.

SIR BRIAN LANGSTAFF: And at that stage hepatitis A had not been identified. That took until 1973. Hepatitis B wasn't identified until -- well, the earliest, the Australia antigen, is about 1966. Hepatitis C had to wait until 1988 and 1989 before there was any full record of what had been cloned in '88.

So am I right in thinking that what was then used to describe hepatitis was a very general term: serum hepatitis?

A. Yes, you would be correct. They talked about serum hepatitis and infectious hepatitis.

SIR BRIAN LANGSTAFF: And infectious hepatitis is what we now know as A?

A. A and E. But yes, mainly A, you are right.

SIR BRIAN LANGSTAFF: And B and C were serum hepatitis, in effect?

A. Yes, yes.

SIR BRIAN LANGSTAFF: So before the hepatitis B was identified -- and the Inquiry's note of screening was that it took place, or started in 1970, for some donations, 1972 generally in the blood supply in the UK, but before then, presumably, hepatologists, clinicians generally, had become aware of the nature of the hepatitis and what it might involve for the individual suffering from it?

A. Yes, yes.

Q. And was it known then that in some cases hepatitis was very slow to show itself? It might not have icteric phase?

A. No. I think for a long time we thought -- and that would have covered the time after the war -- you know, we really took post-transfusion hepatitis, or serum hepatitis, as indicated going by jaundice, which is a very crude determinant really. Although the Blood Transfusion Service did some very good things, they did stick with that for a bit too long. They looked

at jaundice after their transfusions when the Americans had reverted to doing transaminases afterwards.

SIR BRIAN LANGSTAFF: I was going to ask, at what stage did transaminases liver function tests come in, roughly?

A. Oh, you mean as being available in every context?

SIR BRIAN LANGSTAFF: As being used to determine what problems of a hepatitic sort in the liver?

A. I don't know the answer to that. They must --

SIR BRIAN LANGSTAFF: We can find that out from somewhere else. But it was at some stage during the' 50s presumably, was it?

A. Yes. I think it would be before -- probably before the war actually, but they were still talking about serum and infectious hepatitis during the war. There were some major outbreaks in the soldiers in Singapore area, really massive outbreaks, and it was deemed to be a major factor on who won any battle there, the number of soldiers that went down with hepatitis, infectious hepatitis, at that time, because of the terrible conditions. It was a major proportion.

If you go through -- my hobby is going through reading the war plaques in the cathedrals, and if you read them, most of the -- if you look at the

casualties which are looked at in the Boer War and all these, it would say, you know:

"Killed in action ..."

I don't know. Just for argument's sake:

"... 10.

"Killed by dysentery/infectious hepatitis: 100."

So ten times more. So the outcome of these wars was purely dependent on, you know, how well they could keep their soldiers. You know, very few were hit by bullets or whatever else.

So I think, you know, they were very much aware of all this, and I suspect there were transaminase as well as those crude measures of jaundice being used at that time, but I don't know for certain.

SIR BRIAN LANGSTAFF: The nature of hepatitis which might develop after a transfusion, would that lead in quite a number of cases to cirrhosis?

A. Yes. I mean, the big issue would have been, at that stage, how many are due to alcohol. But the fatty liver related to type 2 diabetes, which is in the next year predicted to overtake alcohol as the major cause of cirrhosis -- alcohol was before, the last few years, that was certainly thought to be the most common cause.

Hepatitis B in the context of the UK was pretty unusual, but the Chinese, of course, as soon as the Australia antigen became available, they noted that 10 or 15% of their population were chronically infected with hepatitis B and they had acquired at birth from their mother. And since immunising at birth, the incidence of primary liver cell cancer, which is in the Far East mainly due to hepatitis B, that has gone down massively once the hepatitis B vaccine was used extensively. And the main cause of primary liver cell cancer now, reflecting the fact that the major cause of cirrhosis -- which is, if you like, the pre-malignant condition -- is now hepatitis C, because hepatitis B has been controlled by vaccination.

We still do not have a vaccine for hepatitis C. It is same problem as we are having with this current pandemic. All of these viruses, hepatitis C and the Covid 2 virus, the SARS virus, they are what we call swarms of viruses. So with hepatitis C there may be, you know, 10,000 or 100,000 virus particles, all slightly different in their genetic structure. And as the immune pressure comes on the virus, then one or two virus particles will find they have an advantage, they can break through the natural antibody response or the vaccine response. And the same is true now of

SARS -- SARS-CoV-2. It is too long a name.

That is a mixture of different virus particles, and when you apply an antibody immune pressure to the virus, you will select out variants, which is going to be our problem with the current vaccines and Covid 2. I don't want to be too pessimistic about it, but I think that will happen.

We were able to show this in the context of hepatitis C by looking at agammaglobulinemics. The envelope of hepatitis C varies massively over to hyper-variable regions, to variable regions in the envelope. This is in a person with a normal antibody response. But if you look at somebody with agammaglobulinemia, who can't produce antibodies, there is no variation in the envelope. So it is the patient's antibody response which selects out the variants.

The same will be happening with SARS-CoV-2. You know, as we put different antibody pressures on the virus, you will be selecting out different variants. And because we have a bigger proportion of our population immune now, then we are selecting out different variants, and hence we had the distinction of having the UK or Kent variants named after us, where we -- because we've had a lot of vaccine, we're

seeing variants come through.

I must say, this is a retired armchair ex virology clinician's view of the world, so ...

SIR BRIAN LANGSTAFF: Just taking that same retired armchair clinician's view of the world, you mentioned a moment or two ago, and earlier you were asked by counsel questions about hepatitis B, you mentioned the effectiveness, at least so far, of hepatitis B vaccine. That, as we understand it, was introduced only as a universal vaccine for children in this country in 2017.

Do you have a view or did you have a view as to whether that, in line with your views about testing for hepatitis C and surrogate testing earlier, should have been introduced earlier?

A. Well, it was introduced in the medical and nursing profession, because it is -- the major incidence, I think, is related to blood contamination either through needle use or because of sexual activity, and I think we do have an extensive programme where people attending sexually transmitted disease clinics are immunised against hepatitis B. That was something that came to the advisory group on hepatitis that I was involved in. We pushed really to get control of that mechanism of transmission in our community. But

outside the sexually promiscuous and intravenous drug users, then the transmission of hepatitis B is not that great in the general population and, you know, I think, therefore, at the earlier stage, probably introducing a hepatitis B vaccine wasn't cost effective.

I think a lot of -- there is now a hepatitis A plus B vaccine. I think, for instance, when university students are going on walkabout, you know, on their gap year, then we recommend they are all vaccinated. So as behaviour changes, then the vaccine strategies change.

SIR BRIAN LANGSTAFF: Thank you very much. That's all I am going to ask.

MS RICHARDS: Sir, I should have confirmed Professor Thomas's counsel has no questions that she seeks to ask.

Professor Thomas, is there anything further you would wish to add to your evidence?

A. Not really. I think -- I don't think -- I have had three different experiences as a clinician really: this one on non-A, non-B, where I did get the impression that the NHS was short of money and was, you know, trying to make it go as far as possible; and then, of course, I was on the new and emerging Virus

Committee when the Swine Flu thing started, and there the mathematical modellers said we were going to lose millions of people and I think we lost about 18,000 in the end. The recommendation that I and others was involved in on this committee was we ought to buy a lot of drugs. There were two drugs which were -- might work against flu, and, of course, that didn't come about. So the Department of Health bought a lot of drugs that they didn't need.

Then most recently I think, you know, it's been a question of, you know, the vaccine versus drugs to treat people. I happen to be working in a little biotech company really making drugs for hepatitis -- making drugs for SARS-CoV-2 with Porton Down, and, you know, again the focus has been on the vaccine and not the individual really, but I think the driver to all of this is that we have never been particularly prepared in the UK, because we don't have any spare capacity in our hospitals, and this isn't original. I mean, everybody has said this, and I think it was true right from the word go with non-A, non-B, where, you know, treatment was expensive and there were financial constraints, and it is the same true today really, but otherwise money is always the root of the problems. I would like to see that we spent a lot

more on the health service so that there was a better level of preparedness really, but then you are going to say, "What are you not going to spend money on?" So that's a problem as well, but otherwise I don't have anything to say.

MS RICHARDS: Thank you. Sir.

SIR BRIAN LANGSTAFF: You described yourself just shortly ago as a clinician first and a scientist second. I think certainly you have shown us a huge amount of both sides of what you have to say, but you also have indicated a third side, which is I think demonstrated by the lectures which you have told us you gave from time to time, in which you explain some of the intricacies of science, and you have helped us to explore some of those intricacies in a clear and helpful way and given us access to some of the information which, if I can say, has probably filled a few gaps, for me certainly, and I am grateful, very grateful, for that.

You have told us, so far as the Skipton is concerned -- given us the detail of how you saw your role and the way in which you applied what, to a lawyer, is familiar territory: the burden of proof on the balance of probabilities.

So thank you for all that, and thank you for

allowing us a day of your time. I think you have had experience of giving this type of evidence over a number of occasions. So thank you for being prepared to do it again to help us in this Inquiry.

A. Thanks for being so pleasant about the whole thing. I must say the chaps setting up are really very effective.

SIR BRIAN LANGSTAFF: Well, we have not I think lost any transmission from you. We have had the odd problem just recently, but only rarely, and so I am very glad that you have that to say about them. So thank you for that too.

A. Thank you, Sir Brian.

MS RICHARDS: Tomorrow, sir, we have the evidence of Mark Mildred, first of all, as chair of the Skipton Appeal Panel, and then we will be starting, after we have completed his evidence tomorrow, with the evidence of Charles Lister as one of the Caxton trustees.

SIR BRIAN LANGSTAFF: Yes. So 10 o'clock tomorrow.

MS RICHARDS: Thank you.

(4.58 pm)

(Adjourned until 10.00 am the following day)

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