Wednesday, 4th November 2020

(10.05 am)

SIR BRIAN LANGSTAFF: Good morning, Professor Hay. Can you hear me?

THE WITNESS: Yes, I can, thanks.

SIR BRIAN LANGSTAFF: I'm sorry we're just a few minutes late starting this morning, but can I tell you what will happen? You're here. You're on a number of screens in this room, in London. You're being seen by a small audience here, and you will be followed by a much larger one out there virtually, following you, just as you are virtually connected with us. We had a couple of problems with sound yesterday on our transmission. I hope they've been sorted, but if you have any difficulties, please let us know as we go along and we'll try and resolve it as soon as we possibly can.

First of all, you'll take the oath. Mary will ask you to do that, and then you will see Ms Richards who will be asking you the questions, and occasionally you might see me if I have one to ask as well. Thank you.

CHARLES RICHARD MORRIS HAY (affirmed)

Examined by MS RICHARDS

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

A. Yes, I can.

Q. I am just going to start by asking you a handful of questions about your career. Picking it up from 1977, you were for a period of months a house physician in haematology at Sheffield Royal Infirmary. Was this your introduction to haematology?

A. Yes, it was.

Q. And then 1977, August '77 to August '78, you were a senior house physician, the Royal Hospital Sheffield. You then worked --

A. Yes.

Q. -- I think for a year as a junior medical registrar in general medicine at St Mary's in London; is that right?

A. Yes, correct.

Q. And then August '79 to August 1982, you were a junior registrar in haematology at the Northern General Hospital in Sheffield?

A. Yes, I was.

Q. That work, I think, was general haematology work, rather than specifically concerned with patients with bleeding disorders?

A. That's correct.

Q. And then you took up a post in August 1982 as a senior registrar in haematology at the -- you described, I think, the Sheffield University hospitals as they

became, but you essentially rotated between Sheffield Royal Infirmary, or the Royal Hallamshire Hospital by then, and the Sheffield Children's Hospital for several years?

A. Effectively, with a six-month stint right at the beginning at the Blood Transfusion Centre.

Q. That was August 1982 to April 1983 at the Blood Transfusion Centre. Was that the centre in Sheffield?

A. Yes. At Longley Lane.

Q. And the director, was that Dr Wagstaff at that time?

A. Yes, it was.

Q. What did your role for those six months entail?

A. Well, this was largely a training course. I was there with another senior registrar, Dr Katie Foreman, and the pair of us spent most of our time doing laboratory practicals and rotating around the different departments of the Transfusion Centre, but we also fielded telephone enquiries with a clinical element from clinicians and labs around the region.

Q. Did you encounter during that period any practice of taking blood from prisons?

A. I think I know what you're referring to, because I mentioned in my statement that I had been told that there had been donations from prisons. By that stage, it had stopped. I'm not sure exactly when it had

stopped. I was told this by the head of the virology department. We rotated through their virology department at one point. And he told me that they had stopped taking donations from prisons when they introduced testing for hepatitis B, and they realised that the vast majority of their positive tests were coming from the prisons, and so they recognised that prisoners were a high risk group, and they stopped taking donations from them.

Now, I was there in '82. The practice of taking donations from prisons had stopped some time before, and I can't tell you exactly when.

Q. But that was in relation to the local area, the Sheffield area?

A. Well, that region, it's quite a big region.

Q. Yes. And then between April 1983 and August 1984, you were in your capacity as senior registrar at the Royal Hallamshire Hospital, and your statement says you were given day-to-day responsibility for the haemophilia service under Professor Preston there.

A. Yes.

Q. Could you explain a little more in -- what in practice that day-to-day responsibility entailed?

A. Well, if patients with a bleeding disorder came in with an acute bleed, I would be their first port of

call, and I also ran the follow-up clinics under supervision from Professor Preston and consequently Dr Mike Greaves.

Q. And did you have any involvement with the home treatment programme during that 18-month stint?

A. Well, I guess I must have done. The patients at that time used to come in to the hospital for -- to pick up their home treatment and take it home. We subsequently arranged a system whereby the Transfusion Service would deliver it to their nearest blood bank so that it was easier for them to pick up and they didn't have to come all this way, because some of the patients lived a long way from the centre. But home delivery is a much more recent innovation.

Q. From August 1984 to April 1985, you were at the Sheffield Children's Hospital. Was that under Dr John Lilleyman?

A. Yes, it was.

Q. And, broadly speaking, what did that entail?

A. That -- well, that was -- it involved some thrombosis and haemostasis, because he looked after the children with bleeding disorders, but also involved the management of childhood leukaemia and, at that time, childhood solid tumours.

Q. Then April of 1985 to August 1986, you were back at

the Royal Hallamshire Hospital under Professor Preston, carrying out similar duties as you had previously; is that correct?

A. Yes.

Q. Then you returned for a further six months to Sheffield Children's Hospital between August 1986 and April 1987; is that right?

A. It is.

Q. And then you had a very brief stint at the Northern General Hospital, undertaking general haematology. I think your statement suggests that might have been just for a few weeks --

A. Yes.

Q. -- before taking up your post in Liverpool?

A. That's correct.

Q. So May 1987, you became a consultant haematologist in Liverpool and director of the Liverpool Haemophilia Centre, or I think it may have become known as the Mersey Region Haemophilia Centre; is that right?

A. Yes, it is.

Q. And you were to start with a sole consultant there?

A. Well, I was the sole consultant with responsibility for haemophilia management. There were two other consultants, and we shared the malignant haematology equally between the three of us. So I was clearly the

busiest of the three.

Q. And then December 1994, you moved from Liverpool to Manchester as a consultant haematologist and director of the Manchester Haemophilia Centre at the Royal Infirmary?

A. Yes, the Manchester Adult Centre.

Q. And that's a post that you continue to occupy?

A. Yes.

Q. Then in terms of membership of relevant organisations, you've been a member of UKHCDO since 1987, I think?

A. That's correct.

Q. And then within that, and leaving aside various working parties which we may come on to at a later stage, you were treasurer from 1992 to 1997, vice chair 1997 to 2005, and chair of UKHCDO 2005 to 2011?

A. Correct.

Q. And you have been closely involved with the National Haemophilia Database. Again, we'll come back to the detail of that, but I understand from your statement you've been director of that database since 2002, and you continue to hold that post?

A. Yes, that's correct.

Q. And then amongst other matters, you have given written and oral evidence to the Penrose Inquiry, and you acted as an expert witness for the defence in the

hepatitis C class litigation?

A. I did.

Q. So I'm going to ask you now some more detailed questions about Sheffield and the Royal Hallamshire Hospital, in particular for that first 18-month period you were there, April '83 to August '84; an important period for the Inquiry's terms of reference. I know, of course, that it's a long time ago, professor, but if you can do your best to assist us.

Can you describe in broad terms what the facilities were at the Haemophilia Centre at the Royal Hallamshire when you arrived?

A. Well, they had a world-class laboratory and were very active in coagulation research. The facilities for the patients were less good. Haematology was based on ward P2. There was a clinical room on ward P2 which was designated the Haemophilia Centre. When I arrived, there was a weekly follow-up clinic for patients with haemophilia, which I did. And at that point, there were no haemophilia nurses. There was only irregular physio input, and there was no joint orthopaedic clinic.

But with the passage of time, we acquired a haemophilia nurse specialist, and we organised joint orthopaedic clinics. And on a grace and favour basis,

we got regular physiotherapy input, so things improved from that perspective. There was very good secretarial support throughout that time.

Q. And the clinical nurse specialist, was that Sister Joy Farnsworth?

A. It was.

Q. And she joined, I think, in around 1985?

A. I can't remember exactly, but that's probably right.

Q. You mentioned the weekly clinic. Your statement refers to there being a weekly discussion that would take this --

A. Well, I mean, if I came across a problem that was either above my pay grade or outside my previous experience, I'd go to either Professor Preston or Dr Greaves for advice. But apart from that, we had a multi-disciplinary meeting once a week before the main ward round of the week. And that would take half the morning, during which we would discuss difficult cases and any policy changes. Eric would give us some feedback from committees he might have attended, and we would discuss the literature. It was a separate meeting actually called the Journal Club where we went through recent papers of interest.

Q. How often did the Journal Club meeting take place? Was that regular or ad hoc?

A. No, that was regular. That was once a week.

Q. In terms of the number of patients with the Sheffield Haemophilia Centre, your statement tells us that -- and you, I think, ascertained this from looking at the National Haemophilia Database -- that in 1983 there were 166 patients who were registered with the Centre.

A. Yes.

Q. We've already touched on the Home Treatment Programme. Was that well established and well under way by the time you arrived in April 1983?

A. My impression is that Sheffield was at the forefront of adopting home therapy. I had assumed that all the other centres were the same. It was only as I recently read through various minutes I realised that some centres had been far slower to establish home therapy. But, to be honest, most of the patients were on home therapy even when I was a houseman in 1977. And certainly by 1983 it was more or less universal, except for the odd patient that never took to self-injection.

Q. And the patients who would have been on home therapy were typically patients with severe haemophilia A?

A. Yeah, either severe haemophilia A or B, or moderate severity with the severe phenotype. There is a clinical overlap. The frequency of bleeding doesn't

correlate as closely with the baseline Factor VIII or IX level as you might expect.

Q. And there was, at that stage, no programme of prophylactic treatment?

A. No, none.

Q. Can I just ask you about the products that were used for treatment at that time. We've looked at the 1983 return with Professor Preston. You've exhibited to your statement a document -- Henry, could we have WITN3289040.

So this is an exhibit to your statement and it sets out products used. Is this material that you have picked up from the National Haemophilia Database?

A. Yes, it is. I certainly couldn't remember all these details.

Q. Okay. And we can see from it, and from, as I say, the return that we went through with Professor Preston, that DDAVP was in use, Professor Preston told us that would be used routinely for mild haemophiliacs; was that your experience?

A. Yes, I think -- this is one of the things I actually remember from being a houseman because I think I actually administered the very first dose of DDAVP that was ever used in that department, because I can remember, as a houseman, the letter being published

from Mannucci, and, because of his interest in liver disease, Eric was very keen to try this.

And he told me to administer it but he didn't tell me how. So I just gave it as a bolus injection, which is something you'd never do now, and the patient went bright red and complained of a headache. It has to be administered slowly.

So it was established in Sheffield, probably earlier than in most haemophilia centres. Because it unlicensed, apart from anything else.

Q. We can see from this list that there were -- NHS Factor VIII was used?

A. Yes.

Q. Then a range of commercial concentrates. So for 1983, by way of example, we can see it's the Armour Factor VIII, Hemofil and Kryobulin, and then FEIBA presumably for those with inhibitors?

A. Correct.

Q. Was the porcine Factor VIII used solely for inhibitor patients as well?

A. Yes.

Q. Then NHS Factor IX for patients with haemophilia B?

A. Correct.

Q. There's also reference to Autoplex. What was that used for?

A. Autoplex was another activated prothrombin complex concentrate similar to FEIBA, manufactured by a different manufacturer, thought to be a little bit more activated than FEIBA but used similarly for inhibitor patients.
Q. Then we can see reference to cryoprecipitate, and Professor Preston has already told us that cryoprecipitate was only used, by that time, to a limited extent.

For what categories of patients can you recall cryoprecipitate being used in '83, '84?
A. Well, predominantly patients with von Willebrand's disease. And I would also expect it might have been used in people that needed very infrequent treatment.
Q. Did you have any role in deciding what products should be used at the Centre?
A. No, not really.
Q. In terms of arrangements for the supply of products, do you know whether the NHS concentrate was obtained from the Transfusion Centre or from BPL?
A. To be honest, I can't remember.
Q. In terms of arrangements for the supply of commercial concentrates, did you have any involvement in those arrangements or do you know what they were?
A. No, to both questions.

Q. And in terms of cryoprecipitate, to the extent it was used, was that obtained from the Regional Transfusion Centre or elsewhere?
A. It was obtained from the Regional Transfusion Centre, and I would imagine that that would have been the case everywhere.
Q. Now Professor Preston has told us and Professor Makris has told us in a written statement that two of Professor Preston's guiding principles, in terms of his approach to treatment, were not to put all your eggs in one basket, so to have more than one source of commercial product?
A. Yeah.
Q. And to keep patients on the same treatment and same batch as far as possible?
A. Yes.
Q. Does that accord with your collection?
A. Absolutely, and I think I've written exactly the same thing in my statement. And to be frank, I've followed that principle ever since.
Q. What did you understand, in 1983, the rationale for that principle to be?
A. There was some weak epidemiological evidence that some patients had had more than one episode of non-A, non-B hepatitis.

Now, you know, these are sort of case presentations. I think it is accepted that some patients certainly did, and we didn't know really whether that was because they'd received concentrate from a different geographical origin or just been unlucky and exposed to another strain. As I'm sure you know at this stage in the Inquiry, there are a number of different hepatitis C genotypes but we didn't know that at the time.

So it was felt that if you kept the patients to a single brand and took some care to make sure that that was the case, they might be less likely to be infected for a second time. And the principle behind not putting all your eggs in one basket is because all of these manufacturers have interruptions of supply from time to time; and if you only had one supplier, you might suddenly find yourself very short of Factor VIII.
Q. Do you know how it was decided which patients would get NHS concentrate and which patients would receive a commercial concentrate?
A. If I did know, I can't remember, to be perfectly honest.
Q. Do you recall whether there were any particular difficulties in terms of the supply of NHS concentrate? Was there enough?

A. Well, there wasn't enough. There wasn't enough nationally. And that's why, as you go through the returns and the minutes of various UKHCDO committees, which I've done recently, but was unaware of way back then, you discover that the proportion of commercial concentrate used in the late seventies and early eighties was going up and up and up, because BPL could not supply enough.

And I can remember that when I was a senior registrar there, they were distributing product on a pro rata basis, depending on how much plasma was sent for fractionation by the local transfusion centre. And I think we got about 40% -- that's my recollection, anyway -- of our requirement, as BPL product, on that basis.

And that actually, was a reflection of the fact that our local Transfusion Centre sent more than average to be fractionated. So that was considered a good proportion. But the problem just got worse and worse because if you look at the amount of Factor VIII that is consumed by the patients, over the years you see that over a 40, 50-year period, the amount used goes up by 7% or 8% every single year until very recently.
Q. And you've exhibited a graph taken from the 1986 annual report of UKHCDO.

Henry, it's WITN3289045.

We can see from this that the top line, which has the circles, gives us the total amount of Factor VIII concentrates used in the period that this figure covers, roughly 1970 until a little bit beyond 1985. And then, as I understand it, the line broken up by triangles shows us the amount of commercial Factor VIII usage, the line which is broken up by crosses shows us the NHS Factor VIII usage. And then the line which has the dark squares shows us the usage of cryoprecipitate. And we can see the use of cryoprecipitate declining whilst the use of the concentrates goes up.

Have I correctly understood this document --

A. Yes.

Q. -- that you have shared with us?

A. Yes, that's correct.

Q. We saw with Professor Preston copies of a handwritten ledger which ran from 1976 to 1981. We haven't burdened you with it, Professor Hay, because it's before you arrived, but it's a handwritten book in which patient details for every attendance are recorded, the nature of the bleed, the particular product given, and the batch number. Can you recall, by the time you arrived in 1983, what, if any, system there was for recording treatments and batch numbers.

Presumably you needed to record batch numbers because you had your policy of trying to keep patients on the same batch.

A. We recorded batch numbers partly for that reason, and partly because if there was a specific problem with a given batch, you could trace who'd had it.

It was very common to get allergic reactions, particularly to plasma or cryoprecipitate but also, to a lesser extent, to the relatively crude concentrates that were being used at that time. And some batches were much worse, and occasional batches were actually withdrawn. And you have presented me with some correspondence with Armour, that I'd long since forgotten, that details how we actually withdrew the small number of bottles of their product that we had at one point.

You know, people still use ledgers like that. I have a ledger like that in my Haemophilia Centre. So if we send product out to a patient, we record all those details in the ledger. If a patient comes in or is having surgery, every dose that they get is put into that ledger.

Q. And in terms of home treatment, I know the programme was already well established by the time you took up your post in 1983 --

A. Yes.

Q. -- but were patients on home treatment generally required to keep detailed records of their usage of product?

A. Um, well, they were supposed to. Compliance with that was variable. There's something called Factor VIII returns. They'd have to fill out a line lease on a form to give details of what they'd used the product for, whether they'd responded, whether there were any side effects, and what they'd used, and they were supposed to return those by post or bring them in when they came in. And that provided useful clinical information because when you're assessing the patient, you'd know how often they were bleeding, which joint they were bleeding into, and you could assess whether they were treating themselves adequately or not, because some patients were very stingy with the treatment. And the actual doses that were used to treat bleeds increased progressively, with an evidence base. Because when we were using cryo, six bags of cryo would be equivalent to, I think, one tiny little 250-unit bottle of concentrate, which is now regarded as a paediatric dose. And that's what the patients were treating themselves with, and they weren't getting a very good response. By the time I came

along in '83, the standard dose was about 500 units and it crept up; today it would be 2,000 units.

Q. Now how frequent were the regular appointments at the Haemophilia Centre in Royal Hallamshire? So not those who were attending to outpatients with a particular bleed but those patients you were seeing regularly.

A. Well, to start with, and assuming those specific problems, they would be reviewed every six months. When HIV came along, we reviewed the patients that we knew to have HIV more frequently, particularly once treatment came along, every three months. The patients had open access to the service. This is a universal arrangement with any Haemophilia Centre, that the patients can bypass the switchboard, in a sense, and phone up and speak to a doctor for advice, or pop into the Haemophilia Centre when they feel the need to do so.

Q. So at a typical six-month routine appointment with the patient, an existing patient with severe haemophilia A, could you just talk us through, to the extent that you're able to, from 1983 and 1984, what that typical appointment would entail? What kind of discussions, what kind of tests?

A. Well, you would ask them about any bleeds that they'd had, and you'd ask them how they'd treated themselves.

If they had returns, you would examine these, because they would give, hopefully, a more accurate view of how often they were bleeding. If you thought that they had non-A, non-B hepatitis, you'd examine their abdomen as well as their joints. You might discuss that, you might arrange an ultrasound if they hadn't had one for a while. And as time wore on, we talked more about HIV.

Q. In terms of decisions about the products they would receive by way of treatment, would your role have been essentially just to continue the status quo or were there occasions when you would be recommending a change of -- or wanting to consider a change of treatment?

A. Well, during that period, we -- following the principles I've already discussed, we more or less maintained the status quo, to be frank, until virally attenuated products came along. There wasn't a great deal to pick and choose between the products that we had available to us.

We did participate in one or two studies of virally attenuated products during that time, as you know from the publications. We tested an Armour product, for example, and you'll have remembered the letter to The Lancet about two patients, both of whom

became quite ill with quite severe non-A, non-B hepatitis after administration of that product.

And then the unit also participated in the multi-centre study of Alphanate, and I was very peripherally involved in that, which you might guess from the absence of my name in the list of authors. A lot of it -- that trial actually took place when I was out of the department, at the Children's Hospital, but I was aware of it at the time.

Q. So if there needed to be a decision to change treatment, whether it's changing to a different concentrate or use of a heat-treated concentrate, would that be something that you would then discuss with Professor Preston or --

A. Well, to be honest, my recollection is that if there were any changes of treatment, he would make the decision. I mean, the decision about Alphanate, which I expect we're coming to at some point, was entirely his, and -- apart from that, there were very few changes of treatment, and where they occurred, they probably would have related to difficulties with supply. Sometimes companies had some technical problem that caused supply issues, and then the patients treated with that product had to change.

Q. And then, in terms of the liver function tests that

you would undertake at the routine outpatient six-monthly appointment, '83, '84, what tests, broadly speaking, would you undertake and what discussions would you hold with patients about them?

A. Well, all of the patients were tested for the markers of hepatitis B, and from 1982 they were all vaccinated. We obviously didn't have a test for non-A, non-B hepatitis at the time but we checked the liver function tests, and these would be plainly transaminases but basically a liver function profile, and we checked their blood count, and probably their electrolytes, and not a lot else. They would have an abdominal ultrasound every couple of years.

Q. And if the outcome of the liver function tests gave rise to any cause for concern, how and when would that be communicated to the patient? Would it be at the next six monthly appointment?

A. Yes, it would be at the next six-month appointment.

Q. And was it your routine practice to tell patients the -- what their test results showed?

A. Well, as far as I recall, yes.

Q. We understand from other evidence -- again, Professor Makris, Professor Preston -- that at Sheffield there were stored blood samples, a system which I think predated your arrival there. What, if

anything, can you tell us about that?

A. Well, these were plasma samples stored in the lab. There would probably also have been samples stored routinely in virology, because they retained samples for three years.

Q. Were those samples taken at every routine appointment, to your knowledge?

A. I don't think so.

Q. Were you, as far as you can remember, ever involved in taking those samples for storage?

A. I presume I must have been.

Q. Can you recall what, if anything, was said to patients about that?

A. No, I can't.

Q. In terms of providing patients with information about non-A, non-B hepatitis, we take first of all the case of a patient who you don't currently suspect has non-A, non-B. What, if any, information would you give a patient in this 1983/1984 period about the risks of non-A, non-B from treatment with factor concentrates?

A. Are we talking about a patient with severe haemophilia?

Q. Yes.

A. Well, by that stage, they'd all been treated with

concentrate, and I think we would have understood that, although we couldn't quantify the risk, there was a very high risk that they'd been exposed to hepatitis C. But what we didn't know was how many of those patients would clear the virus. We now know it's about a third. So we really didn't know whether patients with normal liver function tests were viremic or not. But, you know, we would have said to them that it was a possible risk.

Q. And would you have told them, and if you can remember, would you have told them, do you think, that there was a possible risk of non-A, non-B hepatitis, or would you have also told them there was a possible risk of them developing chronic or serious liver disease?

A. Well, when I first went there, although there were papers in the literature that showed very high incidence of abnormal liver function tests in patients with haemophilia, all the liver biopsy studies up to that point, including Professor Preston's study of 1978, tended to show very mild liver disease, and it was the consensus of opinion at that time that non-A, non-B hepatitis was by and large benign and non-progressive.

Now, we know that that's a very poor generalisation now, but back then, that would have been the consensus.

So I think the patients would have been generally reassured. But as you know from my statement, I made a clinical observation that drew that into question, and we started to biopsy our patients more extensively to find out what was happening.

Q. I'll come back to possibly the consensus and the medical literature in a little while, Professor Hay, but just sticking with the information given to patients, because of the -- as I understand your evidence -- please correct me if I'm wrong -- because of your understanding that it was perceived as a relatively mild and non-progressive condition, patients, is this right, might have been told of the risk of non-A, non-B hepatitis but would have been given reassuring information that it wasn't something for them particularly to worry about?

A. Well, that's right. I mean, I can't speak for other centres. One of the things I think you should recognise about the Sheffield Centre is that because of the longstanding interest in liver disease, it assumed a much higher profile in that centre than I believed to be the case in many others.

Q. Then for patients who were not severe haemophiliacs, so patients who were infrequently treated, or mild haemophiliacs, would there be any different

conversation that you might have with those patients about non-A, non-B hepatitis and its risks?

A. Well, however mild or not non-A, non-B hepatitis was, one didn't want to transmit it. For most of the patients with severe haemophilia, it was probably too late at that point, but patients with mild bleeding disorders required treatment infrequently, and so those patients would have been much less likely to have been already exposed to non-A, non-B hepatitis. And it was the unit policy to try to minimise any further exposure. And so those patients would have been treated with DDAVP if the patient was known to have an adequate response to it, or cryoprecipitate, or they would have had a discussion about the relative risks of non-A, non-B hepatitis.

A lot of the patients who were treated for the first time with some of these agents, and particularly the trials of virally attenuated products, would have had that conversation because one of the problems of DDAVP is tachyphylaxis. That's particularly a problem with haemophilia so that each dose has 40% less response than the dose before. So the response may be adequate for a minor procedure such as a dental extraction, but if the patients are to undergo more invasive surgery, the effective DDAVP would wear off, and the patient would be

exposed to an excessive bleeding risk. So they may have no alternative but to have concentrate or possibly cryo.

Cryo is quite difficult for surgery because you need such huge doses. You might be giving a patient 24 bags a day or more, and very soon you get into the sort of territory where they're exposed to a significant hepatitis risk anyway.

Q. Now, you've mentioned already the use of heat-treated products.

A. Mm-hm.

Q. What more, if anything, are you able to tell us about the Centre's involvement in 1984 in those early uses of heat-treated products? Do you know how it came about, for example?

A. I'm not entirely sure how it came about, but we had previously tried heat-treated Armour products, and clearly the heat treatment was inadequate to exclude non-A, non-B hepatitis. And then Alpha came along with Alpha Profilate, and that needed to be tested in a PUP study, a Previously Untreated Patient study. And that trial was conducted between Sheffield, the Royal Free and St Thomas', I believe, and they put 27 patients into it, of whom 24 did not develop non-A, non-B hepatitis, and 3 did.

So, clearly, that was a big step in the right

direction, but when they ultimately came to market this product, and indeed a number of others, they were marketed as hepatitis-reduced products. Now, people used them partly because of HIV and because it was obviously a step in the right direction, but they didn't think it was the full answer.

Q. As far as you can recall, was the Centre's involvement in the use of these -- the two heat-treated products on a trial basis, was that a response to the risk of hepatitis in 1984, or was it a conscious response to the risk of AIDS?

A. No. Well, the AIDS virus hadn't been isolated. It was very much a response to hepatitis. And there were various commercial companies that were looking into viral reduction, mostly abroad, and these products were not necessarily available to us. But, you know, Behring were conducting clinical trials from 1979, but unfortunately their trial of Humate-P took years and years and years to complete. It's quite difficult to recruit patients, and it wasn't available to us at that time.

Q. Do you know, you may not, but do you know whether, for the purpose of these heat-treated trials, Professor Preston approached the pharmaceutical companies to ask to enroll some of his patients in

them, or the pharmaceutical companies approached Professor Preston?

A. I really don't know. But I would imagine it was the pharmaceutical company approaching him. That is usually the way round it comes. And they may have approached him and the Royal Free because both of those centres had a historical interest in liver disease and had indeed published on the use of virally attenuated products.

Q. I just want to ask you a little about the Children's Hospital. I know you were there for a shorter period of time, from August '84 to April '85 first of all, and then you went back for a further six months, August '86 to April '87.

Just going to put on screen the 1983 return from Sheffield Children's Hospital just so we can see as a matter of fact what products were being used.

Henry, it should be HCDO0000139_004. So we can see here, Professor Hay, it's the annual return for 1983 for Sheffield Children's Hospital: total number of haemophilia A patients treated during the year, 17; no von Willebrand's patients; no carriers. Then we can see cryoprecipitate being used, 1,135 bags in hospital, none for home treatment ... NHS Factor VIII being used, 26,185 units in hospital, 147,622 units for home

treatment. And then a small amount of commercial concentrate, Factor VIII, 5,266 units in hospital, 8,500 for home treatment, and then the other material that we see there is Autoplex.

Actually, we'll just go to the next page, please, Henry, for the sake of completeness, as we don't currently have much information about the Children's Hospital. This is -- then for the haemophilia A patients with inhibitors, we can see that they received predominantly cryoprecipitate, a very small amount of NHS Factor VIII concentrate, and down the bottom of the page, Autoplex. And then if we go to the third page, please, Henry, we see one child patient with haemophilia B treated during that year, and treated solely with NHS Factor IX concentrate. And then there's a handwritten note which tells us that some Factor IX concentrate was used for a Factor X deficiency patient on home treatment.

Professor, that paints a picture, at least for 1983, and I'm afraid we don't have the returns for '84 or '85 at the moment, of a -- predominantly NHS concentrate, a more substantial use of cryoprecipitate than at the Royal Hallamshire, and a very modest role for commercial concentrates.

Does that assist in triggering your recollection of

the products that were used at the Children's Hospital at all?

A. Well, I think they had a very small number of patients with haemophilia, and they were able to use NHS products to a greater degree. Most of the patients with haemophilia B throughout the country were managed with UK Factor IX concentrate because there were far fewer of them. So we were, essentially, self-sufficient in Factor IX concentrate.

Q. And, broadly speaking, what was the role that you undertook at the Children's Centre during those two 6-month placements there?

A. Well, I worked closely with the junior registrar in paediatrics, and we worked as a team. And he was not a haematologist, or she, and we managed mainly patients with childhood leukaemia, childhood solid tumours, and occasionally saw patients with bleeding disorders and outpatients, but it was a much smaller Haemophilia Centre than the adult one.

Q. And were the decisions as to what products to use, therefore, down to Dr Lilleyman?

A. Yes, definitely.

Q. Do you happen to know if the policy or system of keeping a patient on the same treatment and same batch was in use at the Sheffield Children's Hospital?

A. I don't recall.
Q. And do you recall whether you had any involvement in talking to the patients' parents about risks of non-A, non-B hepatitis whilst you were there?
A. I honestly don't remember.
Q. As far as you can recall, did the Children's Hospital have any involvement in or access to the early use of the heat-treated products?
A. Well, I don't think so. You know, when we switched over to Alphanate, my recollection is that the supply was extremely limited and that there was some special negotiation whereby they agreed to supply those centres that had participated in the clinical trials.

I think Dr Mark Winter may have been able to switch his patients because of his close association with St Thomas' because I don't think he participated in a clinical trial. But to start with, there certainly wasn't enough of the stuff to supply the whole of the UK.
Q. Now, can I just ask you more generally about how you would keep up to date with literature publications in the early '80s. You've already told us about the Journal Club.

What magazines, as in medical journals and publications, would you read in the early '80s?

A. Well, I got The Lancet, The New England Journal of Medicine. I was a member of the British Society of Haematology and therefore got the British Journal of Haematology. I was not yet an ASH member, so I'd have to go to the library for the -- for blood. And, oh, yes, I was a member of ISTH, so I got Thrombosis and Haemostasis which was the journal of the International Society of Thrombosis and Haemostasis.

And those would be the journals I would read regularly, but if someone pointed me at an article or it came up in discussion in another journal, one might go to the library and take it out.
Q. Prior to 1987 when you became a member of UKHCDO as a director at Liverpool, do you -- did you have access to the reports that were produced for UKHCDO meetings by, for example, Dr Craske or the Hepatitis Working Party, or access to the minutes of the annual meetings or the Reference Centre Director meetings?
A. No.
Q. So your knowledge of what was being said by UKHCDO to the extent that you -- it was disseminated to you, would it have been by Professor Preston at, for example, the weekly meetings you've described?
A. Yes.
Q. On the question of what information to provide to

patients about risks, was that something that was covered in your training, either your general medical training or your specialist haematology training?
A. In my specialist haematology training.
Q. So would you have picked up what -- that advice, or -- essentially from Professor Preston, or from others --
A. Yes.
Q. You've described what you referred to as there being a consensus, or an international consensus, in the early 1980s that non-A, non-B hepatitis was relatively benign and non-progressive. Can you assist us with what material you're there referring to to support the existence of this international consensus?
A. Well, there were a number of patients showing incidence of abnormal liver function tests. Some focused on the use of cryoprecipitate, for example, the paper of Kevin Rickard from Australia, others on the incidence after the introduction of concentrate. It was clear that both agents transmitted whatever the agent was that caused it.

There are a whole series of liver function -- sorry, liver biopsy papers. One from, actually, the Children's Hospital, from Professor Lilleyman. Then there was Eric Preston's in 1978 and, more recently, the Stevens paper from Manchester, which we parodied in the title of

my own paper. And Mannucci and Colombo also did liver biopsy studies and they all showed mainly low grade of inflammation or no inflammation at all. So, you know, Mannucci in particular at that time was particularly going around saying that this was non-progressive.

That title, of the Stevens paper -- or Dick Stevens, actually, I think in the British Journal of Haematology 1981, was "Non-A, non-B hepatitis in haemophilia: an overstated problem?"
Q. Professor Hay, we're currently losing the visual sight of you. We can currently see your tie and nothing else. Given the time, it's five past 11, I'm going to suggest we take a break there, and try to sort that out in any event. But it's probably about the right time for a break anyway.
SIR BRIAN LANGSTAFF: Yes, it is. I think you're probably ahead of us in having had a restorative drink during the course of the morning, but we take half an hour now, professor.
A. Okay.
SIR BRIAN LANGSTAFF: So we'll come back at 25 to 12.

By then, I hope we can see more of you than your tie, nice though it is to look at.
MS RICHARDS: Sir, if Professor Hay can be given the usual warning.

SIR BRIAN LANGSTAFF: Yes, what I say to all witnesses, you may be accustomed to this from previous experience, but is this: you're giving evidence you're on oath, you must not discuss what you have said in evidence or what you think -- whatever you think you might be asked about to come in evidence. You can discuss anything else you like with anyone, but you can't discuss your evidence, past or to come, with anyone at all, whoever they are.

Thank you very much.

(11.06 am)

(A short break)

(11.36 am)

SIR BRIAN LANGSTAFF: Professor, we're back in session. I gather that you may have problems perhaps seeing some of the documents. If you need them enlarged just, please say.

THE WITNESS: I will.

MS RICHARDS: Professor Hay, I've been asking you about what you described as an international consensus as to the nature of non-A, non-B hepatitis. You had referred to a number of papers, Mannucci and the Stevens paper, which I understand.

You referred also to the paper co-authored by Dr Lilleyman, and I'm just going to ask for that to go

on screen so we could have a look at that.

Henry, it's OXUH0001751_003. And can we just zoom in a bit closer, please, to the top half of the page.

Is this the paper to which you were referring, Professor Hay?

A. No. I was referring to one from 1975, actually.

Q. We don't, I think, have that. In relation to this paper, was this a paper that you were aware of at the time?

A. I don't remember it.

Q. Don't worry. In that case, I won't ask you anything further about this particular paper.

Could we then have on screen, Henry, BART0002487. Again, if we could zoom in to the top half of the letter so we can see what it is.

Professor Hay, this is a letter -- I don't suggest you would have seen this at the time. It's a letter dated 27 April 1979, and it's from Dr Kernoff, who, as you've already referred to, had a particular longstanding interest in hepatitis, to Dr Colvin.

Henry, can we go to the second page, please. Could you zoom in on -- can we have the whole of that second paragraph, thank you.

You'll see there's a paragraph, professor, beginning "Types of therapeutic material available".

Then if we go about two-thirds of the way through that paragraph, there's a sentence beginning "The clinical reason ..." Actually, I'll pick it up just before that to make sense of it.

"Not only is commercial concentrate expensive, but there are both clinical and moral reasons for preferring the NHS material. The clinical reason is the growing awareness of the probability that commercial concentrates have a higher risk of transmitting non-A, non-B hepatitis than NHS material. This is a serious disease with long-term consequences which, as far as is known, is at present much less common in the UK than in those parts of the world -- particularly the USA -- where donor blood for commercial concentrates is collected."

Now, I'm not asking you, professor, about the -- whether there was a different risk from NHS and commercial concentrates. But just in terms of Dr Kernoff's characterisation of non-A, non-B hepatitis, he describes it as a serious disease with long-term consequences. Was that your understanding in the early 1980s and that characterisation of non-A, non-B hepatitis?

A. No.

Q. So you would not have characterised it as -- would you

disagree with serious or long-term consequences or both?

A. Well, I think the long-term consequences were unknown. And, I mean, it clearly is a correct statement, as we now know it, but at that time, the long-term consequences were not known. I think that was part of the problem. The liver biopsy studies that had been published were all looking at the early stages of the disease. And there was a consensus forming around that time that this was not a serious problem.

Q. Other than the papers to which you've referred, so I think you've told us about Mannucci in '82, the Richard Stevens paper in '81, and you referred to a Lilleyman paper, 1975, which I'm afraid we don't have available at the moment --

SIR BRIAN LANGSTAFF: There's also the Australian paper from Rickard.

MS RICHARDS: Oh, yes. And an Australian paper.

Are those the sources of your understanding that there was an international consensus, or was it your training, or discussions, or something else?

A. Well, it was partly my training, but I just highlighted some of the papers. I mean, I think there are about 300 references in my antithesis, but those are perhaps the most important.

Q. And what about Professor Preston's own 1978 work? What was your understanding in 1983 of what that paper showed?
A. Well, it showed a variety of different types of hepatitis, histologically, which included mostly relatively low grades in inflammation.
Q. Sorry. Included relatively ...?
A. Mostly relatively low grades of inflammation.
Q. Can we just have a look at that?

Henry, it's PRSE0003622. If we could zoom in on the top half of the right-hand column, please, Henry.

So we've got the paper there; I know you're familiar with it. Professor Preston, September 16, 1978. We have the title of it there, "Percutaneous liver biopsy and chronic liver disease in haemophiliacs". Then the summary refers to:

"Liver biopsies being carried out on eight symptom-free patients under Factor VIII cover. A wide spectrum of chronic liver disease was demonstrated, including chronic aggressive hepatitis and cirrhosis."

Then if we go to the second page, please, just the table at the bottom of the page. I'm not proposing to go through the detail of it with you, professor, but we looked at it with Professor Preston, and he set out what he was referring to by reference to the term -- the

various terms there set out.

Is it -- do you say that this paper supports a consensus that non-A, non-B hepatitis was mild and non-progressive?
A. Well, it's certainly less supportive than some of the others because there are two cases of cirrhosis there. But apart from that -- you know, and I'm not sure exactly how these patients were selected either, because the two cases of cirrhosis may have had physical signs that led to their liver biopsies.

But the papers of Mannucci showed only one case of cirrhosis, and he referred to it as the non-progressive course of non-A, non-B hepatitis, and I think that similar findings from the paper of Stevens et al.
Q. What we also see from this table, as well as the two cases of cirrhosis, are two cases of chronic aggressive hepatitis, which was characterised for us by Professor Preston as being more serious and significant than chronic persistent hepatitis was then understood to be.

Do you disagree with that characterisation?
A. No. It's now known as chronic active hepatitis. In non-A, non-B hepatitis, or rather hepatitis C, it can progress to cirrhosis, though there are also instances

of it going back to chronic persistent hepatitis.
Q. Professor Hay, the paper by Mannucci may be said to lend some support for your view of how non-A, non-B hepatitis was understood at least by some.

Do you maintain your view, however, that that was the consensus view, as opposed to there being potentially a range of different views emerging in the literature?
A. Well, there's always a range of views, but I think the consensus view was that it was relatively benign and non-progressive.
Q. You referred in your statement to one professor using the term "a biochemical curiosity" about non-A, non-B hepatitis, or about the liver function abnormalities. Who was that, professor, and when was that, roughly?
A. That was Professor Sam Machin. That would have been about 1983, '84, when I was chatting with him about our findings. And he expressed surprise that we were still interested in this liver disease because he said it was a biochemical curiosity. Naturally, by that stage, I would have violently disagreed with that view.
Q. By 1983, 1984, you would have disagreed with that view?
A. Yes.

Q. And what was it that led to your own personal realisation that non-A, non-B hepatitis was not benign and non-progressive?
A. Well, I observed a patient in clinic who came along and told me he'd been admitted to the local hospital, having sort of gone to sleep. And he gave a very vague story. His wife was with him. But I examined him, and he had clear physical signs of cirrhosis of the liver. But he was one of the patients with chronic persistent hepatitis previously reported by Professor Preston. And our understanding was that that particular histological appearance, which is a very mild inflammation, not chronic active hepatitis, was thought to be benign and non-progressive. So this was clearly a very odd thing. He was relatively elderly, but he progressed from chronic persistent hepatitis in the late '70s to full-blown cirrhosis with hepatic encephalopathy, which implies a degree of hepatic failure in the space of only six years.

So I brought this to the attention of Professor Preston and Dr Triger, who was the hepatologist, and they agreed that this was a remarkable observation, and they agreed that we should be monitoring our patients more closely with liver biopsy.

Q. Doing the best you can, was that 1983 or 1984?
A. I think it may have been late 1983.
Q. If we just look at the paper that was then published in The Lancet in June of '85. Henry, it's PRSE0004229. And if we zoom in on the bottom half of the page, Henry.

This is the paper co-authored between yourself, Professor Preston, Dr Triger and Dr Underwood. "Progressive liver disease in haemophilia: an understated problem?"

I'm just going to read the summary for the benefit of those following:

"In an eight-year study of 79 unselected patients with haemophilia who had received clotting factor concentrates, there was evidence of chronic progressive liver disease in at least 17 (21%). Eight patients had chronic active hepatitis, and nine had cirrhosis, five with oesophageal varices. Histological evidence suggested that non-A, non-B hepatitis was mainly responsible, although the influence of other viruses could not be excluded. Serial liver biopsies showed progression from chronic persistent hepatitis to chronic active hepatitis and cirrhosis within six years, suggesting that chronic persistent hepatitis in haemophiliacs is not as benign as hitherto supposed."

And then the last sentence of the summary:

"It's anticipated that liver disease in haemophiliacs will become an increasing clinical problem in the future."

So this was the result of work that had in fact been undertaken over an eight-year period, so prior to your joining.

A. Well, yes, it's an eight-year period because it includes all the data from Professor Preston's earlier study.
Q. And then in terms of the process of undertaking further biopsies, the serial liver biopsies referred to, were you directly involved in that process?
A. Yes.
Q. This tells us that the eight-year study of patients was of 79 unselected patients. How were patients identified or selected for biopsy; can you recall?
A. Well, the patients who had been biopsied before -- who did not have cirrhosis, or at least hadn't had cirrhosis before -- were approached to -- for consent to (inaudible) biopsy again to see if their liver disease had changed. And it was explained to them that we had some doubts about the current view about the natural history of non-A, non-B hepatitis, and we couldn't make any assumptions, and we wanted to know

what was happening with their liver disease, and the only way to find out was to do a liver biopsy. And further patients who had abnormal liver function tests were approached, and a similar conversation took place.
Q. And if we go to the second page, please, Henry, if we look at the bottom half of the page under the left-hand column under the heading "Results", please, Henry.

We can see this is what is recorded:

"Initial biopsy in 34 patients showed chronic persistent hepatitis in 20; chronic lobular hepatitis in one."

Pausing there. Could you just explain for us "chronic lobular hepatitis" as distinct from "chronic persistent" and "chronic active"?
A. I think chronic lobular hepatitis is a similar low grade of inflammation.
Q. Then:

"Chronic active hepatitis in 9, established micronodular cirrhosis in 4."

And then the next paragraph refers to 9 patients having a second biopsy. And we can then see that you set out various matters relating to that, and you say:

"Cirrhosis was present in at least 9 of the 34

patients."

And then we can see the table with the results of the serial liver biopsies. The first biopsy, having shown chronic persistent hepatitis in 6, and then there's 4 in chronic -- showing chronic active hepatitis.

And then the second biopsy showing, as I understand it, that in patients 3 and 4, the chronic progressive hepatitis was now showing to be chronic active hepatitis. Patients 5 and 6 had progressed to cirrhosis. Likewise, patients 8 and 9. Patient 7, perhaps somewhat curiously, had gone from chronic active hepatitis to chronic persistent hepatitis.

Is that a correct reading of that part of the results?
A. Yes, it is.
Q. So is it fair to say that the significance of this paper was the further light it shone on chronic persistent hepatitis and its potential to progress to serious liver damage?
A. Yes.
Q. And then, Professor Hay, for the sake of completeness, we'll just look at the two other applications from the Lancet in 1985 to which you contributed.

Henry, could we have PRSE0004594, please.

If we could just zoom in on the bottom half of the page, please, Henry.

So this is July 1985 in The Lancet, professor, and we can see it's a letter co-authored by Professor Preston, you, Dr Dewar, Dr Greaves, Dr Triger:

"Non-A, non-B hepatitis and heat-treated Factor VIII concentrates."

Is this the letter that you were referring to earlier which talked about the problems experienced with the trials of the Armour heat-treated products in 1984?

A. It is.

Q. And the two patients who developed significant non-A, non-B hepatitis within a fairly rapid period of time?

A. Yes. Quite short incubation, unusually severe.

Q. And then the third article in The Lancet from 1985 is WITN3289051, please, Henry.

And if you go to the next page. In fact if you move to -- if you go down the page, please. Next page, sorry, Henry.

There are two letters entitled "Liver disease in haemophilia". If we zoom in on this one. So this is the second letter, entitled "Liver Disease in Haemophilia", is the one authored by you, Dr Preston, Dr Triger and Dr Underwood.

A. Yes.

Q. And I think you refer to this in your statement. This is the disagreement that emerged, through the pages of The Lancet, between those undertaking the work at Sheffield that we've just looked at, and Professor Mannucci and Dr Colombo.

A. Indeed.

Q. And this letter identifies two possible reasons for difference: the age of the cohort being biopsied and studied; and patient selection.

Is that a fair summary?

A. Yes, I guess so.

Q. Before we leave this, is there anything further you wanted to say about this letter?

A. No, not particularly. I think the significance is that it was not immediately accepted by everybody. And Mannucci argued back, in defence of his own earlier assessment.

Q. I'm going to move on to ask you about the developing knowledge of the risk of AIDS.

SIR BRIAN LANGSTAFF: Well, before you do that, can I just ask you one further question about the consensus.

The title of your article in The Lancet was "... an understated problem?"

A. Yes.

SIR BRIAN LANGSTAFF: And you said that was a parody of

Stevens' article in 1982 --

A. No, it was 1981's.

SIR BRIAN LANGSTAFF: '81, I'm sorry. Where he said, effectively: is it an overstated problem?

A. Yes.

SIR BRIAN LANGSTAFF: Why would he think that it was an overstated problem if the consensus was that it wasn't?

A. Well, he published that before Mannucci came along and published his paper in 1982. So there clearly was some diversity of opinion. But by the early eighties I think the consensus was, oh, well, it's not so much to worry about. And in the seventies people sort of became aware of the problem, and would naturally have been worried about it. We know that hepatitis B can progress to cirrhosis and hepatocellular carcinoma in chronic carriers, for example, so there would certainly have been concerns about the progress of non-A, non-B hepatitis based on theoretical considerations alone. But various live biopsies had been done, and as time went by, they appeared, or at least were interpreted to suggest that, well, maybe this isn't as big a problem as we thought it was. And, you know, I think it's against that context.

So you've got the Stevens paper and then another

liver biopsy series from Mannucci which also, in its title, talked about it being non-progressive.

But the interesting thing is, a lot of this is about interpretation, because even the Mannucci paper, it was about 11 patients, quite a small series to base any sort of conclusion on, and one of those patients had cirrhosis.

So looking at the same data, and I think in our correspondence we point out that to him, you could argue that, well, ten per cent of your patients have got cirrhosis. And we're showing 15 per cent. So why are you arguing the toss?

SIR BRIAN LANGSTAFF: Yes, I see.

So the one thing that seems to be clear, tell me if this is fair, is that there was a significant risk -- sorry, a risk that serious hepatitis might result, but people were at odds over time, views differing, as to quite how serious the risk was. Is that fair?

A. Particularly in the seventies there was probably greater dichotomy of opinion. But by the early eighties I think that they'd settled around thinking, oh, well, it wasn't such a big problem after all. That was my perception, talking to colleagues from around the country, and reading the literature. And

I think it was Professor Preston's perception too, to be honest. But then we started to see more people with more serious liver disease, and the closer we looked, the more we found.

Not everyone with cirrhosis will have physical signs of cirrhosis. They often don't. So it's only if you do a liver biopsy -- or, more recently, we would, of course, do a fibroscan, we have non-invasive methods now, but back then the only way to find out was to do a liver biopsy.

SIR BRIAN LANGSTAFF: Thank you very much.

MS RICHARDS: Professor Preston [sic], can you recall when and how you first became aware of reports of AIDS in haemophiliacs in the States?

A. Well, the very early 1980s, when there was a run on pentamidine, CDC recognised that they were issuing far more pentamidine, which is a treatment for pneumocystis pneumonia, than they expected.

Now, pneumocystis pneumonia is a type of pneumonia that haematologists are very familiar with because we see it in our immunosuppressed patients with lymphoma or leukaemia. But it's not common. It's caused by an opportunist pathogen. And the CDC in the United States realised that this was -- this sudden increase was being used in a different risk group, and it was predominantly

being used for homosexual men who were presenting with pneumocystis pneumonia. And it was at that point, I think 1981, maybe '82, that they really began to realise that there was a new disease out there.

Q. We know there were reports in July 1982 in the MMWR publication produced by CDC of PCP observed in haemophiliacs?

A. Yes.

Q. This was shortly before you'd be taking up your post at the Blood Transfusion Service?

A. Yes.

Q. Would the MMWR have been a publication that you saw or had access to at that time?

A. No.

Q. Can you recall what, if any, discussion there was in the six months you were at the Blood Transfusion Centre, so from August '82 to April '83, about the risk of AIDS and AIDS as a potential blood-borne virus?

A. I don't remember anything about that.

Q. Do you recall reading the article in the New England Journal of Medicine January 1983 by Jane Desforges about AIDS and haemophilia? We can put it up on screen.

Sorry, it's a slightly unfair question without

showing you the document.

It's PRSE0002410. It's New England Journal of Medicine, January 1983, "AIDS and preventive treatment in haemophilia".

And if we go to the bottom paragraph, please, Henry, we can see there it refers, third line down:

"Reports from the Centers for Disease Control include three haemophiliacs among cases of ... AIDS."

And then there's further discussion about the presentation of AIDS. And then if we go over the page the last paragraph, please, left-hand column, Henry, it says:

"The fact that haemophiliacs are at risk for AIDS is becoming clear. The use of cryoprecipitate will minimise this risk, the current home infusion programme needs to be revised."

And then the last two sentences:

"Physicians involved in the care of haemophiliacs must now be alert to this risk. Preventing the complications of the present treatment may have to take precedence over preventing the complications of haemophilia itself."

Leave aside for a moment, professor, the reference to use of cryoprecipitate. Was this is an article, as far as you can recall, that you saw at the time?

A. I can't remember. I don't remember the specific article. I think I was aware of the three cases in the US, one way or the other, during 19 -- certainly by 1983.

I can't remember exactly when I started to take the New England Journal. I started to --

Q. Now, we also --

A. -- take the Lancet, however. I don't think I was taking the New England Journal at that point.

Q. Now we know that in around December of 1982 there were reports of a baby, a San Franciscan baby, 20-month old baby transfused with platelets developing the AIDS syndrome, and we know that that is something that, as a matter of fact, came to the attention of Professor Preston, along with an update of what the current position was in terms of AIDS and haemophiliacs at a meeting in late January 1983.

Now that, of course, is whilst you're still at the Regional Transfusion Centre and three months before you joined the Royal Hallamshire.

When you joined the Royal Hallamshire in April 1983, can you recall what discussions there were about AIDS and the risk of AIDS being transmissible by blood or blood products?

A. I can remember that it was recognised that it was

beginning to appear in patients with haemophilia. And that we assumed that it was caused probably by a virus. There were some contrary hypotheses, but they never gained much traction. So I think we assumed it was caused by an unknown virus, and we didn't know what the risk was.

We assumed that all blood products might carry it, I think, because it was beginning to appear in the UK population as well. By "UK population" I mean the general population.

Q. We also know that in around March 1983 Haemophilia Centre Directors were asked to look out for symptoms or signs of AIDS in their patients and report back to Dr Craske if they detected any such signs.

A. They did.

Q. Do you recall whether -- is that something you were asked to undertake as part of your routine care of patients, to look out for signs of AIDS, and if so, alert Professor Preston?

A. Yes.

Q. And then did you, as a matter of fact, identify, as far as you can recall, in any of the patients at the Sheffield Centre at that time, any such signs?

A. I don't remember.

Q. Then you've produced a document from June 1983.

Henry, could we have WITN3289041. If we just zoom in on that.

This the letter of 24th June 1983 sent to Centre Directors by Professor Bloom and Dr Rizza, following a special meeting of Reference Centre Directors, and it sets out in the two numbered paragraphs there two general recommendations.

If we just look at those recommendations, it says at (1):

"For mildly affected patients with haemophilia A or von Willebrand's disease and minor lesions, treatment with DDAVP should be considered. Because of the increased risk of transmitting hepatitis by means of large pool concentrates in such patients, this is in any case the usual practice of any Directors."

Was that the usual practice at the Sheffield Centre at that time?

A. It was already the usual practice because of non-A, non-B hepatitis.

Q. And then in (2), it says:

"For the treatment of children [and we can leave that aside] and mildly affected patients or patients unexposed to imported concentrates many Directors already reserve supplies of NHS concentrates (cryoprecipitate or freeze-dried) and it would be

circumspect to continue this policy."

So taking, first of all, mildly affected patients, this is a suggestion that if you have an existing policy of treating them with cryo or NHS concentrates, continue. Did this lead to any change of approach for your mildly affected patients? Or were you already predominantly using DDAVP?

A. I think we were already doing that. And as you've already pointed out to me, at the Children's Hospital they were using predominantly cryoprecipitate or NHS concentrate at that time.

Q. And then in terms of patients unexposed to imported concentrates, was there any particular approach or policy agreed at the Sheffield Centre in relation to that category of patients in light of this letter?

A. Well, I don't think it changed very much, because we already had a policy of keeping people to the brand that they were on. So, you know, if people had been treated exclusively with British products, that would continue.

Q. But if it was a patient who was a new patient, maybe -- I don't know that you didn't come across any in your time there -- a new patient who hadn't previously been treated with imported concentrates, would they have been started on NHS concentrates or

would it have depended on availability?

A. It would have depended on availability, I think.

Q. And then other than the continuation of the existing policies you have described and the early use of heat-treated products, which you've already referred to, were there, as far as you know, any other changes to the approach to treatment at the Sheffield Centre in '83, '84 in response to the risk of AIDS?

A. I can't think of any. I think we deferred some surgery.

Q. Do you know whether that would have been 1983 or '84 or indeed later?

A. I'm not sure, to be honest. But I seem to remember that some surgery was deferred. That happened in quite a few places.

Q. Was any consideration given to a suspension, at least on a temporary basis, of the Home Treatment Programme?

A. Well, I think this was discussed. I can't say exactly when because, as you've pointed out, the suggestion did come up in the literature occasionally, so it wasn't something that was completely ignored. But it was certainly Professor Preston's view, and I think that this was commonly the case, that this would be resisted by the patients, was not recommended by the Haemophilia Society or the World Federation of

Haemophilia.

And I think what people were trying to do -- this comes across in some of the minutes involved with Professor Bloom -- was to try to balance out the risks. Now, on the one hand, if you go back to cryo, you have an immediate supply problem because cryo wasn't being very much produced, and the requirement for Factor VIII had tripled during for the previous decade.

So I'm not sure there would have been enough cryo. Certainly, you would have had to turn the Transfusion Service on its head to suddenly produce a whole lot of cryo, which would not have happened overnight. Then you would have reverted to the life expectancy that had pertained before that event of concentrate.

Now, the introduction of cryo improved life expectancy enormously, because in the pre-treatment era, it was 10 to 15 years, and it increased to about 40. Actuarial methods published by Charlie Rizza et al suggested that we'd nearly normalised life expectancy.

So changing back to cryo would have been expected to have reduced life expectancy, maybe not dramatically, but to some extent. And they were trying to balance this up, because this was all knowledge that was known

at the time. Trying to balance this up against the big unknown.

Now, of course, if we'd known then what we know now, the argument for switching to cryo would have been very much stronger. But they were trying to balance a known change in life expectancy on the one hand against an unknown effect of AIDS. And I think at the time they were doing that in 1983, there was one patient reported with AIDS, and by the following year it had gone up to about three, as far as I can recall.

So, you know, numerically, the problem didn't appear big, but there clearly was an enormous degree of uncertainty. Because the natural history of HIV had not yet unfolded, and we had no idea how many patients were affected.

Q. Can I try and unpick some of that with you, professor?

A. Yes.

Q. First of all, as far as Sheffield is concerned, can you recall whether there was -- whether positive consideration was given, whether at the weekly meetings you've described or otherwise, to reverting to cryoprecipitate, either in whole or in part? Was there actual discussion about that in Sheffield?

A. Yes, there was.

Q. And what was the forum for that? Was that on

a regional basis, or was it in the weekly meetings you've described?

A. Well, we certainly discussed it in the weekly meetings. Whether it was more widely discussed, I don't know. But Professor Preston rejected it. As far as I'm aware, John Lilleyman rejected the idea as well. And they quoted other colleagues' consensus documents. You know, I think it was considered fairly widely.

Q. You've raised one possible practical impediment, that of supply.

A. Yeah.

Q. Now, we've seen evidence, for example, from -- and I'm not suggesting you would necessarily have been aware of this at the time -- from an October 1983 UKHCDO meeting, where Dr Chisholm in Southampton said that she had unlimited supplies of cryoprecipitate -- her problem was getting commercial concentrates -- and some other directors agreed. So in --

A. I think it would have varied from region to region because this is a product that's produced by the local Transfusion Centre, and it's not just used for haemophiliacs. It was also used for the treatment of disseminated intra-vascular coagulation and other acquired bleeding problems. But, you know, it varied

from centre to centre.

When I got to Manchester, for example, admittedly much later than this, they'd stopped manufacturing cryoprecipitate altogether, and I had to actually ask them to start making it again.

Q. Do you know whether Professor Preston or indeed Dr Lilleyman approached the Sheffield Regional Transfusion Centre, or Dr Wagstaff, to explore with them the possibility of increasing production of cryoprecipitate?

A. If he did, I don't know about it.

Q. Then in your statement, you've set out a number of concerns about possible reversion to cryoprecipitate, some of which you've touched on in your oral evidence. You'd said in your statement that cryoprecipitate was incompatible with home therapy. We've heard evidence that -- of a number of haemophiliacs in the course of the 1970s receiving home treatment through the use of cryoprecipitate.

Would you accept that incompatible is perhaps an overstatement?

A. Well, I wasn't aware of that at the time. I am aware of it now. But what I would say about that is that it was a minority of centres that had some pilot -- what I'd describe as pilot projects of home therapy with

cryo, because logistically it was quite challenging. You'd need a minus 40 to minus 60 freezer. A domestic freezer would not do. These are sort of great big bulky things. They're quite expensive. Not everyone would have room for it. Many of the patients actually complained about the amount of space their Factor VIII concentrate took up in their fridge. Some patients had to have more than one domestic fridge. But at least the concentrate you could keep in a domestic fridge, whereas with cryo, it has to be delivered from the Transfusion Centre, without breaking the cold chain, to the patient's home and then stored in a minus 40 freezer. And even as home therapy, there would be a delay in being able to treat yourself because you've got to defrost it and draw it all up. It's much more difficult drawing up, you know, 6 or 12 bags of gloopy stuff than it is having concentrate.

So, yes, there was limited use of cryo for home therapy, but it depended on a number of factors, and it was never widespread.

Q. Yes, well, I mean, we've heard a range of evidence in relation to that, so I'm not sure the evidence we've heard would support the characterisation of it as pilot in terms of its usage in the '70s.

A. Well, I honestly don't think there were large numbers

of patients on home therapy with cryo, and most centres weren't doing it at all.

Q. In terms of your own direct experience, is this right: that you would have had no experience or little experience of patients in Sheffield on the home therapy with cryoprecipitate because by the time 1983 came along, it was all concentrates?

A. Well, it isn't just that. When I was a houseman, there were still patients switching from cryo to concentrate and going on to home therapy, so I did have some experience of routine treatments. I also came across it as a medical student when I did my paediatrics, but they never had a home therapy programme with cryo in Sheffield.

Q. And then you've said in your statement and again in your oral evidence this: that changing to cryoprecipitate or no treatment would dramatically increase the risk of haemorrhagic death, decrease life expectancy dramatically, and lead to more rapid deterioration of haemophilic arthropathy.

Now, if we take out the reference to no treatment, professor, what's the evidential basis for your assertion that changing to cryoprecipitate in 1983 would have dramatically increased the risk of death as a result of haemorrhage?

A. Well, haemorrhage at that time was the commonest cause of death in severe haemophilia, and the life expectancy estimate, before the introduction of concentrates, was about 40 years, whereas I think Rizza et al, based on the early returns to Oxford, the National Haemophilia Database, calculated that life expectancy was about 67, 68.

Q. Is the answer to my question that the factual or evidential basis for that assertion is Dr Rizza's paper?

A. Yes.

Q. If a return to cryoprecipitate had been not for haemophiliacs for the rest of their natural lives but for a period of time -- a year, 18 months -- in the knowledge that work was being done on heat-treated products, that work was being done to identify what the virus was, that there might be a test for the virus, what basis is there for believing that a change to cryoprecipitate for a year or 18 months would dramatically increase the risk of death or decrease life expectancy dramatically?

A. Well, I mean, it would have -- for that period of time, they would have been more at risk of dying from haemorrhage. Now, okay, yes, it's a limited period of time, and that would reduce the danger, but for most

patients it would have meant reverting to hospital-based treatment.

Now, this was one of the great advantages of concentrate because we knew that with haemophilic bleeding, the earlier you treated it, the less damage is done. So when the patients had the treatment at home, they were told: if you think you've got a bleed, treat yourself immediately. It may not be a bleed, but, you know, you have a lot of personal experience, and they would be able to do so.

Now, if they had to come into hospital and have cryo, it affected the way that they behaved so that, you know, if they lived a long way away, they'd think twice about coming in to hospital. They would make sure they were certain it was a bleed before they considered treatment, so by the time they arrived in the hospital, they often had an advanced haemarthrosis. And then someone would assess them, decide they needed cryo, send to the blood bank. The blood bank would send the cryo. Then they'd defrost it. Then they'd draw it up, and then they'd administer it. So by the time you'd finished, there's been a delay of a number of hours.

Now, with a haemarthrosis, the result of that is that there is far more joint damage and the haemarthrosis takes a lot longer to resolve, but I think

you can probably argue that doesn't make a difference to life expectancy.

If, on the other hand, they develop a headache, which may just be a headache or it could be the early signs of an intracranial bleed, then a delay can be really life-threatening. So if somebody with haemophilia phones up the Haemophilia Centre and says, "I've got this headache and it won't go away," you'd say to them, "Give yourself some Factor VIII and come in to the hospital." Or maybe you'd organise transport. But they would have treatment before they left their house, in that instance, and that could be a matter of life and death.

Q. On this hypothetical scenario, the delay that you're describing could have been dramatically reduced by the provision of cryoprecipitate as a home therapy, to be used --

A. Yes.

Q. -- perhaps not on a regular basis but in the event of an emergency such as that which you describe?

A. Yes, but I would suggest that -- well, you know, home therapy with cryo happened in a few centres, a relatively small number of patients. Setting it up on a national basis, with the purchase of all those refrigerators, some patients wouldn't have had any

room for it, would have been a major undertaking that couldn't have happened very quickly, I would imagine. When do you suggest that they should have done that?

Q. Professor, I'm exploring with you what options were considered and what difference they might --

A. Okay.

Q. What the practical impediments might have been. Do you --

A. I think in most centres, they considered that it was not a suitable product for home therapy, for logistic reasons.

Q. Do you accept or agree that the question of whether to take that risk of possibly delayed treatment in the event of a headache, or to take the risk of having less than ideal treatment for other bleeds and possible risks of joint damage was a decision for the patient to take, rather than for the physician to take for the patient?

A. That's an interesting philosophical question, because the big problem is that these decisions were being made on the basis of very little information. And, you know, even the guidelines that came out were not as evidence based as we like our guidelines to be because they were based on opinion, and that opinion was very poorly informed because there were so many

reasonable questions about AIDS, and subsequently HIV, that just were not known. A lot became clearer once the tests became available.

Q. Were patients, as a matter of fact, at the Sheffield centre [audio disruption] --

A. -- questions --

Q. -- told --

A. And I think it would have been an order of magnitude more difficult for the patients, because, you know, the conversations were to be relatively uninformed.

Q. Sorry, professor, we had a slight problem with the Internet connection then but I think we got your answer.

A. Okay.

Q. Were patients, as a matter of fact, from -- in the time you were at Sheffield, so from April 1983 onwards, told of the possible risk of AIDS from the continuing use of factor concentrates?

A. I do recall having conversations with the patients about AIDS. It was widely reported, patients did ask about it. And to be honest, we weren't able to quantify the risks.

Q. Were patients routinely given that information, such information as you had, or was it only discussed with them if they raised it with you?

A. They were routinely given that.

Q. And what kind of information in 1983, '84, do you think they were given?

A. I think they would have been told that there was some evidence that recipients of blood or blood products were developing AIDS but that there were very few cases, and they were probably told that, as far as we could see, the risk was relatively small at that time. I think that was the general view.

Q. Was any patient, as a matter of fact, given the choice to revert to cryoprecipitate?

A. I don't recall that.

Q. Were there any attempts made in '83/'84, to acquire more NHS concentrate in view of what was thought to be the increased risk of AIDS associated with commercial concentrates?

A. Er ... there may well have been, but I don't recall. There was always a supplier problem with NHS concentrates. We could never get enough of them.

Q. Was any consideration given, as far as you can recall in this '83/'84 period, to using porcine products for non-inhibitor patients in response to the risk of AIDS?

A. Very little. There's several things you need to know about porcine. I mean, in actual fact, the one

clinician who used porcine Factor VIII for non-inhibitor patients during this period was my predecessor in Manchester, who actually published a paper on this. And he had used it for surgery in little-treated patients to avoid the risk of non-A, non-B and, possibly, whatever the AIDS virus was.

But the product that was available at that time was, by modern standards, an intermediate purity product. It's essentially a concentrate of porcine Factor VIII. If you use it in a non-inhibitor patient, a significant portion of patients will develop antibodies which are specific anti-porcine antibodies, and then you won't be able to use it again. And some will develop transfusion reactions with the product. And it intended to make your platelet count fall in a very predictable way, because it also included quite a lot of porcine von Willebrand factor which causes human platelets to aggregate.

Q. Was the predecessor at Manchester who used that, are you referring to Dr Wensley?

A. I am.

Q. And do you recall the use of porcine product in the way that I've just discussed being actively considered at Sheffield by Professor Preston or is it that it

wasn't considered and you're suggesting reasons why it might not have been considered?

A. I can't remember it being discussed or considered. I only found out about Dr Wensley much, much later.

Q. You've referred in your statement, and indeed Professor Preston made reference to them, to there being a meeting or meetings involving a number of patients at the centre to discuss the risk of AIDS or to discuss AIDS. Can you recall anything further about those meetings and how they were set up, and what kind of matters were discussed?

A. Sorry, you broke up a little bit there.

Are we talking about the Journal Club or the multi-disciplinary meetings?

Q. No, I'm sorry, neither. My apologies, Professor Hay.

Professor Preston told us about there having been a meeting with patients, and your statement I think also reflects that: a larger meeting, not a one-to-one patient meeting, a larger meeting or meetings to which patients were invited to discuss AIDS.

A. Yes.

Q. What, if anything, can you recall about those?

A. I didn't -- I can't remember actually attending these. They were meetings between Eric and any patients who wanted to come along and I believe he discussed with

them what was known about the issue at the time. And he had a number of them as the state of knowledge progressed, particularly once we had a test. Because the state of knowledge progressed very rapidly after that.

Q. In terms of the Children's Hospital, and you returned -- you were at the Children's Hospital for your first 6-month period, August '84 to April of 1985, can you recall what, if any, discussion there was with the parents of patients at that hospital about the risks of AIDS?

A. I can't recall. I'm sure we will have discussed it with them. But I can't remember the nature of those discussions. I'm sure it would, amongst other things, have come up during the regular reviews.

Q. Do you or would you agree that the parents of children who were receiving factor concentrates that might expose them to a risk of AIDS were entitled to be told of that risk?

A. Yes, of course.

Q. Now you'd then returned to the Royal Hallamshire Hospital in I think April 1985. By that time, what was the position in terms of the use of heat-treated products?

A. Well, I think Eric had switched over -- in, I think,

December of the previous year -- as many patients as he could to Alpha Profilate, on the basis that there was some evidence of a model virus, which they thought would be similar to what turned out to be the causative agent of AIDS, being heat labile.

So it was quite a leap, to be perfectly honest, but, you know, I was giving the patients the benefit of the doubt. This was the safest product we had available to them. And there was no direct evidence that it was safe from the HIV point of view, but he thought that it might be.

It clearly wasn't completely safe, but from the point of view of non-A, non-B hepatitis. But we didn't know at that time that the HIV virus was more heat labile than the hepatitis viruses, so it was actually easier to eradicate it using heat treatment methods that might be inadequate for hepatitis.

Q. We know that in December 1984, and you've exhibited the statement to the relevant document, UKHCDO produced a set of recommendations which included the recommendation to use heat-treated product.

Your statement says, at paragraph 48.4, that most Haemophilia Centres were obliged to continue to use some untreated concentrates until sometime in 1985. Was that because of insufficient supplies of the

heat-treated products?
A. Yes, and some centres still had a preference for British products, which was impossible to satisfy, because BPL had been so slow to even begin to address the issue of heat treatment. And what they did, as I recall, was to withdraw their unheated products and stick them in an oven and heat-treat them, and send them back.

And the first heat-treated product that they produced in that way was essentially insoluble, and we couldn't use it. So there was, in effect, quite an interruption in supply of British products, and it took a while to sort out.

And people were scratching around for any heat-treated product they could find. A lot of it was unlicensed. And there wasn't enough of it.
Q. Do you know how long it took into 1985 for Sheffield to no longer be using untreated concentrates and to have exclusively heat-treated concentrates?
A. I can't remember exactly. I have actually looked at the annual returns for that year, from the database, in anticipation of this question. I couldn't get a clear view from that either, because it was quite clear that a variety of products were used during the course of that year. And that is despite the fact

that Alpha was supplying preferentially those Centres that had participated in their clinical trial.
Q. Then in relation to those with haemophilia B who had I think at Sheffield consistently been treated with NHS Factor IX concentrate --
A. Yes.
Q. -- do you have any recollection as to the point in time at which heat-treated Factor IX concentrate was available for the Sheffield patients?
A. Well, I think that they had to use AlphaNine, if my memory serves me correctly, which was commercial. Because it was later in '85, I think, that 9A heat-treated UK Factor IX became available, and in the interim the only heat-treated Factor IX available would have been commercial.
SIR BRIAN LANGSTAFF: If it helps, it was 2nd October 1985, that all the Factor IX issued by BPL was heat treated. That's my note.
A. Thank you.
MS RICHARDS: I wanted to ask you about the process of testing patients for HIV, HTLV-III, at the Royal Hallamshire and then, to the extent that you can recall, at the Children's Hospital.

The testing at the Royal Hallamshire, from material that we've seen, probably began in late 1984,

and you'd have been at the Children's Hospital at that stage. But we understand from Professor Makris that the testing was on the basis of the stored samples.

Do you have any knowledge yourself of the arrangements that were made for testing patients at the Royal Hallamshire for HTLV-III in late '84, or early '85?
A. Well, I wasn't there when it all started. I didn't remember it being from stored samples. I'm sure that stored samples were tested because that gives you historical background and a basis on which -- from which to tell the patient not only whether they've got HIV but when they contracted the infection. It's useful to know.

But my recollection is of patients coming up, having a chat, and then having a blood sample taken.
Q. So is your recollection that patients were told in advance that they were going to be tested for HIV, HTLV-III?
A. Yeah. I mean, it may well be that Professor Preston sent stored samples off to Professor Tedder in London at a point when the test was very experimental. And the difficulty with that sort of thing -- I mean, it was difficult enough once the test had been validated because when you sit down with the patient and you

discuss the result, the implications of the test are not fully known. So it's quite a difficult conversation.
Q. When you returned to the Royal Hallamshire in April of 1985, as far as you can recall, had all the patients been tested and informed of their diagnosis by then, or was that an ongoing process in which you were involved?
A. I was never very much involved in that. I think it was an ongoing process. I don't think they had stored samples on everybody, but it was undertaken as fast as they could, I think. And Professor Preston spoke to the patients in his room, I think, before and after testing.
Q. Your statement suggests, in terms of the numbers who were found to be infected with HIV, that 24 had HIV, of which one was under the age of 18. We have slightly different figures from Professor Makris. Not radically different, but slightly different. Can I ask, where has your information come from to --
A. Well, my information -- you can imagine, I couldn't remember those numbers, so I went to the National Haemophilia Database. He may have a different source.
Q. And you're not in a position, from the information you had, to break it down by reference to whether it was

haemophilia A or B, von Willebrand's and
-- (overspeaking) --
A. No.
Q. Did you have any involvement in the testing of family members for HIV at the Royal Hallamshire?
A. I honestly don't remember. Family members would have been offered a test, particularly since it was recognised from a very early stage that the causative agent could be sexually transmitted.
Q. The process of giving information to patients about their diagnosis and its significance, that was undertaken, was it, by Professor Preston, rather than by you?
A. Largely. Though, you know, obviously, I would have come across these people in clinics, and naturally they would have wished to discuss it there too. And as far as partners are concerned, we were all encouraging patients to bring their partners with them, to follow-up visits, and certainly to any discussions about testing.
Q. And what, if any, knowledge do you have about seroconversions from heat-treated products for patients at the Royal Hallamshire?
A. I don't think there were any. Though I am aware that there was an Armour product used in other centres that

was withdrawn because some patients contracted HIV from those products, and I think that was the subject of litigation, but I don't think that involved Sheffield.
Q. You were asked in your statement whether work was undertaken at Sheffield to establish the time period during which patients seroconverted, and you said in your answer:
"Some stored samples were available in Sheffield from some but not all patients which enabled the approximate date of the initial infection to be determined. I recall that most had been infected in 1982 to 1984."
Do you know when that exercise of trying to establish the dates of seroconversion was undertaken?
A. It would have been undertaken very early on, at the time of initial testing, possibly before the test was fully validated.
Q. And do you have any further information about that process and what it showed?
A. No.
Q. Then in relation to the Children's Hospital, so you were at the Children's Hospital during that last part of '84 and first part of '85 when testing was becoming widespread.

What, if anything, can you recall about the process of testing the children at the Children's Hospital for HTLV-III?
A. I don't think they had any stored samples. Professor Lilleyman would have seen all of the parents individually and arranged testing.
Q. So did you have any involvement in the process of informing parents that their children had tested positive?
A. It's the sort of thing that I think John Lilleyman would have wanted to do himself.
Q. Can I move on, then, to Liverpool, where you took up your post in 1987.
Who was it that you succeeded as director at the centre?
A. Dr BA McVerry.
Q. Can you give us an outline of the facilities that the Liverpool centre offered in 1987?
A. Well, the patients came along to the laboratory, which was in the Duncan Building, which is annexed to the main Royal Liverpool Hospital building, on the third floor, and there was a large clinical room in the middle of that laboratory, and that was the Haemophilia Centre.
We had secretarial support, and I had a junior

member of staff that rotated through thrombosis and haemostasis as part of the internal hospital rotation. But there were no other staff. And there was no haemophilia nurse, no counsellor, no physiotherapy, and there were no joint clinics.
Q. Was it a Reference Centre by 1987?
A. No, there weren't any Reference Centres. Well, there were, but Liverpool was never a Reference Centre. That was one of the designations from the earlier days. It did subsequently become a Comprehensive Care Centre when those were -- that title was designated.
Q. And your statement tells us, and again I think you've taken this from the National Haemophilia Database, that in 1987 there were 162 patients registered at the centre.
A. Yes.
Q. What was your understanding of the approach to treatment at the centre that had prevailed in the early part of the 1980s? What products typically had been used? Do you know?
A. I think I've listed some of them. But basically a mixture of BPL and commercial products.
Q. Had there been much use of cryoprecipitate at Liverpool?
A. I don't think so.

Q. Do you know whether it had been a user of DDAVP for mild haemophiliacs and others?
A. I think latterly, yes.
Q. What, if any -- sorry, by the time you got there in 1987, were all the concentrates that were being used heat treated?
A. Yes.
Q. Do you know whether any of the Liverpool patients had seroconverted from heat-treated products?
A. Not as far as I'm aware.
Q. I think you raised a concern shortly after you arrived at Liverpool, with Ms Spooner, I think, at Oxford, that you discovered that there were quite a few patients who were not registered with Oxford. Is that right?
A. That's correct.
Q. Do you know how that had come about?
A. Well, I think they were just not very conscientious about reporting patients. I think it was a voluntary database, and I think patients commonly weren't reported. When I took over the database in 2002, there were only 16,000 registrants, and we now have well over 30,000. And I don't think that that is reflecting the birth of new patients; I think it's reflecting previous historic under-reporting,

particularly of the patients with mild bleeding disorders.
Q. Do you have any recollection of what kind of proportion of patients had not been registered with Oxford prior to your arrival in '87?
A. Well, in the Liverpool centre I got the impression it was over 50%.
Q. Over 50%?
A. Yes.
Q. And when you then completed I think you called them notification forms or something like that in your correspondence with Ms Spooner --
A. Yes.
Q. -- were those providing -- or what kind of information was then provided about the patient to Oxford in those notification forms?
A. Well, the basic notification form just reported the patient's identifiers and their diagnosis and the severity of the diagnosis.
Q. Did you report, either in relation to that cohort of patients or more generally, to Oxford, the HTLV-III or HIV positive status of your patients?
A. Yes, you'll come across all of this when you read my still not completely written report that goes at the end of this statistical report, but there was -- there

were separate forms for reporting the details of HIV. And as you've already observed, Dr Craske initiated that process, and it continued for a number of years. So yes, I filled those forms out as well.
Q. And did you tell your patients that you were providing that information about them to Oxford?
A. I think that I did.
Q. What did you learn at Liverpool about how patients had been told that they were HTLV-III positive?
A. Well, the patients told me. I had very little information from Dr McVerry himself. They told me that they had been informed by post.
Q. So they learnt they were HTLV-III positive by a letter from the centre?
A. That's right.
Q. And in terms of the numbers of patients at Liverpool who were found to be HTLV-III positive -- I've just lost the reference to the numbers -- I think you've said in your statement, in Liverpool 43 patients had HIV, of whom four were children.
A. Yes.
Q. And you've taken that from the National Haemophilia Database rather than any Liverpool records?
A. I have.
Q. Okay.

MS RICHARDS: Sir, I note the time. Is that a convenient point at which to stop?
SIR BRIAN LANGSTAFF: Yes, it is.
We take a break for lunch. Two o'clock, if you please, professor. Two o'clock, everyone. I'll see you then.
THE WITNESS: Thank you. Thank you.
(1.01 pm)
(Luncheon Adjournment)
(2.00 pm)
MS RICHARDS: Professor Hay, I was asking you about Liverpool and your work there from 1987 onwards.
You were now, as director, responsible for decisions as to what products to use. What were the existing contractual arrangements, can you recall? Was it something that the previous director had done directly, or was it done regionally?
A. Well, it was what the previous director had done. It was done originally because it was a regional Haemophilia Centre. It covered Mersey Region and parts of North Wales.
He contracted on -- well, through the hospital purchasing manager, to purchase Factor VIII, and that would have to be agreed -- or Factor IX -- and that would have to be agreed with the commissioners.

Q. And was that then an arrangement that you took over? So for the years that you were director at Liverpool, did you undertake the decision-making process and the arrangements for the acquisition of commercial products?
A. Well, I agreed which products we should use, subject to the approval of the commissioners who paid for it.
Q. And by "commissioners" you mean the hospital authorities, effectively; the fund holders?
A. Yeah, the fund holders. We had a manager, and we would negotiate with each of the district health authorities what they would pay.
Q. Your statement says you continued with the policy that had been operated at Sheffield, of using a single brand of concentrate per patient, if you could?
A. Yes.
Q. And what was the basis for the continuation of that policy?
A. Well, it just seemed generally good practice. It made it easier to trace back if there was a problem with a specific batch of a product. It made it easier to handle any product recalls that might occur and also made it much easier to discuss with patients if there needed to be a change.
Q. Were you --

A. And we had to make changes from time to time, as newer, better products came along, or old products were withdrawn.
Q. Were you able to ascertain, either from the patient's records or from your own discussions with patients, what kind of information they'd been given in the preceding years about the risks of non-A, non-B hepatitis?
A. The medical records before I arrived appeared poor and were uninformative, so the short answer is no.
Q. So did you then discuss non-A, non-B hepatitis from '87 onwards with your patients when you saw them?
A. Yes, because we were monitoring for it, and, yes, we would.
Q. In relation to risks of AIDS, HTLV-III, HIV, were you able to ascertain, again either from records or from your discussions with patients, what information they'd received before they were tested about the risk of AIDS?
A. That was never very clear to me. I obviously spoke to the patients. They maintained that they didn't know very much about it and that when they had been informed of the result, they were not given very much support because there were very few staff. But nonetheless.

Q. And you told us already that they had been informed of their result by letter.
Did you ascertain or become aware of whether they'd even been told they were being tested for HIV?
A. I can't remember.
Q. Was there any system of stored samples at Liverpool?
A. Before I arrived, there had been, apparently. And I made specific enquiries about that with Dr McVerry without any result. I suspect that some of the patients were tested from stored samples, but I was never able to obtain the results of those tests.
Q. So it would follow, I think, from that that you don't have any information about the periods of time during which Liverpool patients seroconverted?
A. That's right. I mean, that's why I made those specific enquiries. There was nothing left for me, and he didn't answer my letters.
Q. Do you have any recollection as to how many, if any, family members, partners, wives and so on of patients were HTLV-III positive?
A. I can't remember, but we certainly offered testing to all partners, and we encouraged partners to attend follow-up clinics with their husbands.
Q. Now, how was the care and treatment of the patients at Liverpool with HIV, how was it organised from 1987

onwards through to 1994 when you left?
A. Well, I managed them largely myself, although, increasingly, I consulted with my STD colleague, Dr Carey, and occasionally with infectious diseases consultants, but they were based at Fazakerley Hospital, which was the other side of Liverpool.
Q. What kind of support in terms of counselling or social work support was available?
A. Well, when I first arrived, there was nobody but me, so I had a lot of -- initially quite difficult consultations with these patients who, as you might imagine, had many, many questions and required a great deal of support. It was a pretty awful time, and there was a great deal of uncertainty, and we all had a great deal to learn about HIV still.
From 1988, AIDS money came along, and you'll have seen the article in the Haemophilia Bulletin about the team that they managed to put together, so we then had a counsellor, a social worker and a haemophilia nurse specialist, who was quite a senior nurse, and they also provided a great deal of pastoral support which was most certainly needed.
Q. And in terms of the AIDS money, can you just tell us what that was and where it came from?
A. Well, I think it was recognised by the Department of

Health that a lot of Haemophilia Centres, particularly those north of Watford, did not have the wherewithal, in terms of staff and specialisation, to deal with this new problem adequately.

You know, I only learned about the existence of haemophilia nurses when the Haemophilia Society sent me to one of their weekend annual residential seminars. I'd never even met a haemophilia nurse until I went along to one of those. So many Haemophilia Centres didn't have haemophilia nurses or the sort of full infrastructure that we now take for granted.

So the Department of Health made some money available which was distributed at a regional level for that sort of infrastructure.

Q. And was that money made available on an annual and continuing basis, or was it time limited?

A. My understanding was that it would be continuing.

Q. Do you know how the allocation was calculated?

A. I don't -- I can't remember. I do remember having conversations with the regional Health Authority where they said that they had received an allocation; what was my shopping list? So I gave them a shopping list, and they agreed to pay for it.

Q. Did you experience difficulties in obtaining funding

for treatments for HIV and AIDS as those treatments became available at Liverpool?

A. Not unduly. Whenever any new treatments came along, you would always find that the regional Health Authority or the local health authorities didn't have the money, so there was often a delay. But HIV had such a high profile that I don't remember having inordinate difficulty getting the funding for that in particular.

Q. Now, HCV testing became available whilst you were still at Liverpool.

As far as you can recall, when did the process of testing for hepatitis C start and for how long did it go on?

A. It started when the second generation of hepatitis C antibody tests became widely available, which would have been during the course of 1991. Since the testing was not clinically urgent -- and so the patients weren't all brought in in a big wave but tested at the next follow-up clinic, and then they would be informed of their result at the follow-up clinic following that, unless, of course, they wanted to know the result more quickly.

Q. Had there been any use of the first generation of tests by you at Liverpool?

A. No.

Q. When the second generation tests became available and you started the process of testing, did you tell patients that you were going to test them for hepatitis C and seek their consent?

A. Well, I think I did tell them, because the context of testing them was in the clinic, and this was a new test. And, you know, they would also have had conversations before then about non-A, non-B hepatitis. So those that had abnormal liver function tests, or who had been treated with concentrate in the past, we would have expected to have a positive test.

Because this is an antibody test, it doesn't tell you whether you've got hepatitis C, only that you've been exposed to the virus at some stage in the past. So, you know, you'd say to them that you wanted to test them for hepatitis C, and you would say to a lot of them that you would expect the result to be positive.

There were some where you didn't know whether it would be positive or not, and those were the patients who had been very infrequently treated in the past.

Q. You described that as being a process that was undertaken at the regular outpatients appointment. So a patient would come in for a scheduled appointment,

you'd arrange the hepatitis C test, and then you'd tell them the results at their next appointment.

What about those who were not attending for regular appointments because, for example, they were infrequent bleeders?

A. Well, they were brought up to clinic once a year at that time. Of course, now we follow more and more of them by telephone. But they were brought up once a year, and so it would take longer to test them. But over a 12-month period, you would have picked all of those up.

Q. Can you recall whether there was a cohort of patients who you were unable to trace who were effectively lost to follow-up and untested?

A. You find that in every centre, and we would chase those up very actively, particularly when we were wanting to test them for hepatitis C or any new agent for that matter.

Q. And then when patients were given their results, those who were tested positive, what information at that stage, 1991/1992, did you provide to them about the significance of the positive diagnosis?

A. Well, you would have already made some sort of assessment of their liver disease. These are -- if they had chronic transaminitis, indicating chronic

liver disease, they would have had things like liver ultrasound and so on, and so you would be in a position to say whether they had probably or not got severe liver disease or not. And you would have indicated to them that a proportion of patients can go on to develop cirrhosis or hepatic carcinoma, but it was still the minority of patients; that other patients go for a very long time without progressing and that, in general, the rate of progression is relatively slow (some people don't progress) and that we would have to monitor their liver disease, but they might need to see a hepatologist and that we were beginning to experiment with treatment to eradicate the virus.

Q. The first treatment that was available was interferon.

Were you using interferon for your patients at Liverpool, so prior to 1994 when you moved on to Manchester?

A. Yes. Once it was licensed.

Q. So it wasn't used on any kind of named patient basis; only when it was licensed.

Were you involved in any clinical trials of interferon?

A. No, I didn't participate in any of the trials. I only used it when it was licensed.

Q. Can you recall what information you gave to your patients at Liverpool about interferon, both in terms of what was understood to be its prospects of success and in terms of side effects?

A. Well, that varied with time. We had already got experience of using interferon for some haematological malignancies. So, you know, when we started to use it, it wasn't without any experience. And interferon on its own was often not too badly tolerated. I should emphasise the "not too badly" because most people got flu-like symptoms and fatigue.

When you started to combine it with other drugs such as ribavirin, and then when you moved on to peg interferon, the side effects were generally much worse. And I would have a consultation with the patients, often several, and I would strongly encourage them to bring their wife along to the consultation so that they would hear about the side effects straight from the horse's mouth. And I would warn them that depression was an extremely common side effect and sometimes persisted for weeks or months after the treatment finished; that most patients suffered serious fatigue during the course of the treatment; some lost weight, and that it was extremely common, for the patient, however sweet natured they

might have been before they went on to treatment to become extremely tetchy and get into arguments for no good reason.

It's particularly important to have the wife present for those sort of discussions so that they understood that that really was the case and that the husband wasn't spinning them a line, because these psychological side effects were very serious. Some patients committed suicide with the depression. The number of patients who expressed suicidal ideation to me ... and the family had to endure this as much as the patient. There are families whose marriages have broken up because of those side effects.

And then there were the haematological side effects, in that some patients became neutropenic, that's a low white cell count, or anaemic. Some required transfusions or the administration of growth factors to support their white cell count. So that you could optimise the dosage, because it became apparent that if you started to compromise with the dosage because of haematological side effects, that reduced the response rate.

And of course, you would discuss the response rate, which -- really depending on the regime that you're using and the patient's genotype. And of course we

started with interferon alone for six months. And that was successful in some. We were doing that before we were able to genotype the patients, but it had a very low success rate.

They then moved to interferon alone for about 12 months, and then it was combined with ribavirin.

The combination with ribavirin for 12 months was much more successful, particularly, it turned out, in people who did not have genotype 1. With genotype 1, that regime had no better than a 40% response. And for patients that -- that sort of information is really important, because you'd describe the side effects and many patients would say, "Well, I'm going to hang on and wait for something better"; which I think, to be honest with you, wasn't unreasonable. And you wouldn't twist their arm. And these consultations would often be multiple. Because of the slow rate of progression of the hepatitis C, there was no clinical urgency for most of them to start treatment.

If they were developing serious liver disease, that might be another matter and then you would involve a hepatologist, a hepatologist might well already be involved, and their arm would be twisted a bit more. But ideally, you wanted to treat them before they developed serious liver disease, to prevent serious

liver disease from developing. And also because the response rate was better in people that didn't have cirrhosis.

Q. For those patients who were already HIV positive, how often between 1987 and 1991, 1992, would you be seeing the HIV positive patients in clinics?

A. At least every three months.

Q. Those who then also tested positive for HCV, so those who were co-infected, were there additional arrangements put in place for them to be seen, or hepatology inputs sought at Liverpool?

A. Well, Professor Gilmore, our only hepatologist at the time, had his clinic immediately next to mine, and was always an extremely available, helpful colleague. And so we had a lot of joint consultations. And if I was -- if I was concerned that a patient was developing more serious liver disease, I would ask him to manage the patient jointly. I would also consult with him about the changing indications for treatment during that time, and follow his protocol for selecting people for treatment, because there were national protocols for selecting people for treatment that the hepatologists developed, and he would pass on to me.

Q. And for those patients who were not HIV positive but

had now been diagnosed by you with hepatitis C at Liverpool, what were the varying arrangements for them to be seen? How frequently were they seen? Would it depend on their liver disease?

A. It depended on their liver disease but, as a broad generalisation, they were seen every six months.

Q. Did you experience difficulties in Liverpool in obtaining funding for treatment for hepatitis C?

A. There were usually delays in getting funding. We couldn't really apply for funding until the product was licensed. I had developed a contractual structure for my patients with haemophilia, which was a cost-per-case contract, so I charged for each individual patient, and that contract specifically excluded certain extras such as interferon, because if you didn't exclude it, they might expect you to pay for it out of the allocation that they'd already given you, even though there wouldn't be enough money to do that. So you would have to make a separate application for funding for interferon.

And what usually happened was, when this came along it would be viewed by the health authority as a financial pressure, they would not have planned for it in advance, and there was usually a delay of a few months whilst they found the money for it. But once

there was a process in place, you would make an application and you would get the funding for treatment usually quite quickly. That was the process.

Q. You left Liverpool in 1994. Do you know who took over as centre director at that point, in Liverpool?

A. It was Professor Cheng-Hock Toh.

Q. And then you moved to Manchester. You've given an indication in your statement of the number of registered patients in Manchester in 1994, and the number there was 525. Is it fair to say that Manchester was one of the largest Haemophilia Centres in the UK by 1994?

A. Yes. Again, I think there was probably under-reporting, or under-registration of the patients, but I think it was probably about the third largest Centre in the country.

Q. Now you mentioned your predecessor there, Dr Wensley. Is it right that I think there had been a period after Dr Wensley's departure, before you took up your post, when Dr Lucas was director?

A. That's right. A period of about two years.

Q. Again, could you give an outline of the facilities that you found at Manchester when you arrived in 1994?

A. There was a small Haemophilia Centre attached to the

laboratories, which included a storeroom, an office, two consulting rooms, and a waiting area. And in terms of staff, there was a nurse counsellor, two other haemophilia nurse specialists, and that was it. Oh yes, a clinical assistant.

Q. Do you have any knowledge of what the approach to treatment had been at Manchester prior to the universal availability of heat-treated concentrates in the mid-eighties?

A. I think in Manchester they had been particularly slow to switch people to home therapy. I had patients who say that they hadn't had concentrate until 1982, and they had had a strong preference for BPL products.

Dr Wensley was jointly employed by the Transfusion Service, and only 50% employed by Manchester Royal Infirmary. They had used cryoprecipitate more than most centres for longer than most centres.

Q. Do you have any sense of how much commercial concentrates had been used? A rough proportion as between NHS and commercial in the early eighties?

A. I don't know. I'm not sure.

Q. Did you have any sense, when you arrived there, of what the Centre's approach had been to the response to the risk of HIV and AIDS?

A. Well, I get the impression that Dr Wensley was quite

careful about this. He had, after all, been probably the only clinician in the country to have used porcine Factor VIII in a patient lacking an inhibitor to minimise that risk, and he had -- their whole approach to therapy was very conservative. And that continued to be the case, to the extent that one of the things that really worried me when I took over was that I could see that, despite having the -- being the third largest Haemophilia Centre in the country, its budget was tiny, and the patients were using an average of only 25,000 units per patient per year, for severe haemophilia.

Now that compares with about an average of 300,000 units per patient per year today. But even back in 1994, it was, by a margin, the smallest amount being used.

Q. And was there any bank of stored samples, plasma samples at Manchester?

A. None that I was aware. I believe that they had had stored samples at some point, but I wasn't aware of any when I took over.

Q. And what, if anything, did you learn about how patients at Manchester had been informed of their diagnosis with HIV?

A. Well, again, I was led to believe by the patients that

they had been informed by post.

Q. And did you know, do you know whether those patients had been aware that they were being tested for HTLV-III?

A. I'm not sure about that.

Q. And you tell us in your statement, again -- well, I don't know whether this figure is drawn from the National Haemophilia Database or your own records, but you've said that there were 83 patients HIV positive, of whom ten were under the age of 18.

A. That's derived from the National Haemophilia Database.

Q. Do you know, of those patients in Manchester, the proportion that were severe haemophilia A patients as opposed to moderate or mild?

A. I couldn't tell you.

Q. Do you know how many haemophilia B patients were infected with HTLV-III?

A. I'm not sure. But it would have been a smaller proportion, given that they were treated only with UK concentrate and HIV spread later into the British donor population.

Q. Do you know whether any work had been undertaken in Manchester to ascertain the dates of seroconversion?

A. Yes. This was in the notes, and it was apparent for some patients, and when they were told about their

HIV, their -- or had subsequent discussions with my predecessors, they were told when they had been infected.

Q. Do you know what the date range was?

A. It was mostly 1981 through to '84.

Q. And do you know whether there had been any seroconversions at Manchester on heat-treated products?

A. I don't think so but I would not swear to it. I don't think any of the products that had been known to transmit HIV after heat treatment had been used in Manchester.

Q. Were there partners or other family members who had been infected with HIV at Manchester?

A. Yes.

Q. Do you recall roughly how many?

A. A handful.

Q. When you arrived in 1994, how had the care and treatment of the patients with HIV been organised?

A. In various different ways. Dr Wensley and Dr Lucas looked after the bulk of them. Some patients had gone to more -- a small handful had gone to North Manchester, where they have infectious diseases doctors with an interest in HIV.

Q. And what arrangements did you then follow over the

next few years from 1994 as director?

A. Well, the patients who attended North Manchester continued to do so. Patients left in Manchester, I continued to look after, increasingly with input from STD, as the subspecialty of HIV specialist developed, and then we developed a joint HIV clinic, particularly once HIV treatment became a little more complicated. Because in the early days there were only one or two drugs, and then more drugs came along and -- to start with, they were all reverse transcriptase, inhibitors, which -- you know, all working in the same way, then other classes of antiretroviral drugs were developed, with different modes of action, which lent themselves to combination treatments.

None of this was as effective as one might like until triple therapy came along in 1995. Because a lot of the patients who had had treatment in the early years, because it was, by modern standards, suboptimal, that developed some degree of resistance, and it was, as much as anything, dealing with that resistance that made it increasingly necessary to involve more specialist help in their management.

Q. And what was available in Manchester in 1994, by way of counselling or social work support?

A. Well, we had a part-time social worker. We had a nurse counsellor, and the nurse counsellor would go to patients' homes and see them in the department.
Q. Hepatitis C testing in Manchester. When, as far as you are aware, did that begin?
A. I think it began in late 1991, and most of it was conducted in 1992.
Q. Do you know whether patients had been told in advance that they were being tested for hepatitis C and their consent sought?
A. It's my understanding that they were tested in much the same way as we tested them in Liverpool and that they came along to clinic. And this was mentioned to them as an additional test.
Q. And by the time you were there in 1994, as far as you are aware, had the testing process been undertaken for all the patients?
A. I assumed that it had not been conducted for all the patients, and I reviewed that each time I saw a patient for the first time.
Q. And so were there --
A. Sorry. There were patients referred in to me also from other centres where I had assumed, since, you know, I'm thinking about 198 -- [audio disruption] assumed that they might have been tested, and it

turned out that they hadn't been, so I didn't make any assumptions.

As you've already pointed out, patients with mild bleeding disorders are seen less frequently and that, in its own right, may have led to them being tested later. So if I couldn't find a test, I'd assume that they hadn't been tested and I would test them.
Q. And when would that patient be told their test results? Would it be at a special appointment or the next routine scheduled appointment?
A. You would discuss that with the patient and at the consultation, because as I think you'll have noticed from my statement, when I arrived, I discovered that the mild bleeders were not followed systematically. This was quite a common practice back in the day. It was never my practice, nor the practice in any Haemophilia Centre I'd ever worked in. But in many cases, because they only need attention every few years, they would be told their diagnosis and said, "Well, you know, if you need surgery or you need advice, contact us and we'll see you."

Whereas the problem with that was that we'd suddenly get a communication from a surgeon in some hospital without a Haemophilia Centre who wanted to operate on one of your bleeders whom you didn't know because they

hadn't been seen for ten years. So I sent an appointment for all of these patients, and of course everyone moves an average of every seven years, and so we didn't have current addresses for a lot of these patients, so it was quite a struggle to bring those patients in.

And they needed chasing up, partly because things had moved on, and partly because they needed to be tested, and in some cases you couldn't make any assumptions about HIV either. I don't think I picked up any new HIV positives in that way, but we certainly picked up some who had hepatitis C.

When you asked those patients, "What have you been treated with in the past?", they'll say, "Well, I had an injection of some clear fluid back in 1972, but I can't remember what it was, or I never knew."

So you couldn't make any assumptions about what they'd been treated with and had to assume that if they'd had any sort of treatment, it was potentially infectious, and so you just tested them all.
Q. What information would you then typically give a patient who you were telling for the first time at Manchester that they had hepatitis C?
A. Well, I would already have had a conversation when I tested them, particularly if they'd -- were one of

the mild bleeders who hadn't been followed up because those patients would have had zero awareness of hepatitis C. So they really would need a conversation about "I'm going to test you for hepatitis C. From what you've told me of your treatment history, I either think the risk is very low or I don't know". And I would arrange to see them sooner, not in six months' time, and maybe in a couple of weeks if they were clearly anxious about it.
Q. Whether at Liverpool or Manchester, these kind of discussions with patients about testing them for hepatitis C and then telling them their result and giving them information about their condition, would those typically be recorded by you in their medical notes?
A. Well, they might be very briefly. I have to admit that I've never been good at writing in the notes, and my letters are usually more informative and would often be copied to the patient.
Q. What approach did you take, whether at Liverpool or Manchester, in terms of notifying patients' GPs of their diagnosis of either HIV or hepatitis C?
A. Well, we would write to the GP. In the case of HIV, it was considered very sensitive, so there were conversations with patients about whether to write to

their GP or not. Almost none of them would object to you writing to the GP, and we would argue -- well, not argue, but we would discuss with the patient that the GP might attend them in an emergency and would really need to know.

I did have one patient who lived in Wales who explained to me that he lived next door to the doctor's receptionist, and whilst they had very good relations with their neighbour, he was understandably worried about confidentiality, and we came to a special arrangement for him because he could see the intellectual reasoning for letting his GP know.

Q. And I think your statement says the special arrangement was that the GP would keep the records at the GP's own house so that the receptionist would not have access to them?

A. That's right.

Q. Did you ever tell GPs of a patient's HIV status without the patient's knowledge and consent?

A. Possibly. I don't know specifically.

Q. What about hepatitis C? What was the approach to notifying GPs?

A. Well, we wrote to GPs every time a patient came to clinic. So we would write to the GP. We would not specifically ask the patient about that. The patients

knew that we wrote to the GPs every time they came, and I could not see why they would object to us letting the GP know.

Q. What were the arrangements made at the Manchester Centre for the care and treatment of patients with hepatitis C from 1994 onwards?

A. Well, historically, Dr Warns the hepatologist had a close working relationship with the Haemophilia Centre and indeed appears as one of the co-authors on the Stevens paper and had conducted a lot of -- well, he conducted all of those liver biopsies in that series.

The non-serious liver disease we largely managed on our own. Though, again, as with Professor Gilmore, we regularly consulted with hepatology about the criteria to be used in selecting patients for treatment. And I would often send the patients to Dr Warnes for hepatology opinion.

Now, back then -- and I've discussed this with people from other Centres too. Back then, there were not so many hepatologists. I don't think the Cardiff Centre had one, at least until recently, for example, in the whole of Wales, which is unimaginable. And because there were not many hepatologists, what hepatologists tended to do was offer an opinion, give you some

instructions and send the patient back.

For those patients who had serious liver disease, my desire was that they should be joint managed with a hepatologist, and if there was any question about whether they should be treated or not, I wanted hepatological input.

Now, when Dr Warnes retired, he was replaced by Dr Harry, I think, who was far more active. And subsequently, she was replaced gradually by up to three hepatologists, and they have basically taken over all the therapy for hepatitis C. They do joint manage all our patients who have serious liver disease.

And throughout that time, the Liver Clinic again was immediately adjacent to our own follow-up clinic, so the patients would often come along to both clinics the same afternoon, and we had -- it was easy for us to have joint consultations. Throughout that time, we had a very close liaison with hepatology.

Q. I think if we put one document on screen. Soumik, it's BART0000735, please.

This is a letter from you to Dr Rejman, the senior medical officer at the Department of Health in 1985. And we can see from the first two paragraphs a problem with funding. You said:

"You were asking us yesterday to let you know of

specific problems that we have encountered in relation to health authorities paying for alpha interferon for the treatment of hepatitis C. Since the Secretary of State for Health has gone on record in the House as saying that nobody suitable for interferon therapy should be denied this.

"I have to tell you that we have encountered consistent problems with two of our Health Authorities, namely central Manchester and Trafford Health Authority. These two Health Authorities take the rather paradoxical view that they were paying for haemophilia services before, and we should just absorb it within our costs, despite the fact that no interferon was prescribed in this practice before the product gained its licence."

It would seem from that that you did experience difficulties at Manchester in obtaining funding for interferon.

A. Yes.

Q. How long did those difficulties remain?

A. Well, we did eventually get it paid for, but we had consistent problems with those two health authorities because I think -- I mean, the hospital's actually in the Manchester Health Authority, but partly because of demand, and I guess the patient population, those Health Authorities are always short of money.

I had -- one of the first things I did when I took over in Manchester was to move from a block contract to a cost-per-case contract on the basis that it would be more difficult for Health Authorities to refuse an individual than a whole group, and because a block contract was open to this sort of abuse.

If you have a block contract, they give you an amount of money that is to cover everything. And then, when a new pressure comes along, they say, "Well, that's your problem." And of course, your block contract will probably not cover all your expenses in relation to therapy anyway. And the whole of this time, we were trying to increase the intensity of treatment to manage the haemophilia better, not to mention increasing expenses in relation to HIV treatment and the treatment of hepatitis C.

To give you some idea, a course of peg-interferon and ribavirin would cost around £14,000 back in those days. And we argued that, to be honest with you, compared with the cost of the haemophilia itself, it was a relatively small amount of money.

Now, what you have here is evidence of the Health Authority still behaving as if you've got a block contract, even though you haven't. So I was trying to stir things up in the background, and we did eventually

get funding. And in fact, when peg-interferon and ribavirin came along, we were able to get funding before the liver doctors were.

Q. I'm going to move on to look at a different issue now, Professor Hay, and to ask you some questions arising out of recommendations produced by UKHCDO in the late eighties and early nineties.

Soumik, can we have on screen, please, WITN3289044.

And if we zoom in on the first half of the page, please. This is a set of recommendations exhibited to your witness statement, professor. This from 1988 and it's the UKHCDO's or the Reference Centre Directors recommendations on choice of therapeutic products.

And I just want to show you a couple of passages and then ask you a question about them. So in the first paragraph, last sentence, it says:

"Whilst it is clear that risk can never be completely eliminated, major advances have been made in risk reduction and physicians are faced with the problem of choosing between therapeutic products of possibly differing risks."

"The purpose of this paper is to present a consensus view of the UK Haemophilia Reference Centre Directors on the relative merits of therapeutic products ..."

And then it says the intention is to update recommendations.

Then if we go to the bottom half of the page, please. It says this:

"It must be emphasised that our opinions about the risks and therapeutic efficacies of different products are based on evidence which is often incomplete, and in many cases unpublished. Despite these problems, physicians necessarily have to make therapeutic decisions in the best interests of their patients, within the resources they have available. It has always been the case in the UK that such decisions have often had to be made without guidance from the regulatory authorities. Whilst this situation is to be deprecated, it is important for physicians to be aware of the legal framework in which they prescribe therapeutic products ..."

And then at the bottom of the page, last two lines, it says:

"It is also important to remember that all manufacturers, including those within the NHS, have an [go over the page] interest in interpreting data concerning their own products in the most optimistic light, and vice versa."

I am not going to ask you about the detail of the

recommendations that then follow, professor, but am I right in understanding that this was the first time the UKHCDO had formulated detailed recommendations of this nature?

A. Yes, I think it was. It's clearly far more detailed than the guidance that appeared in 1983 and '84.

Q. Does it surprise you -- and you obviously weren't a Reference Centre Director at this time, but you were now a member of UKHCDO -- does it surprise you that it took until 1988 for there to be something along these lines: detailed recommendations in which an attempt is made to analyse the risks associated with individual products? It took that long for this to be produced?

A. Well, not necessarily, because prior to the advent of viral attenuation there really wasn't a great deal to pick between the different brands of concentrate. It may well have been that there were differences, but in the absence of testing, you couldn't discern what those differences were. That is to say, the products that were available may have carried different risks but that had been even less well quantified than it was at that point, whereas here we finally have concentrates that have been virally attenuated and purified in different ways, and clinical trials have been conducted to try to evaluate the safety and

efficacy of those products, so there is far more evidence on which to formulate a recommendation. And even so, they are, I think quite rightly, stressing the limitations of the data that they have available to them.

In later evidence they would adopt an even more evidence-based approach to guidance where each recommendation would be given a scoring for the strength of evidence upon which it's based.

One of the big problems assessing the safety and efficacy of therapeutic products for haemophilia is that it's a rare disease. If you look at clinical trials of things like heparin, it starts with -- you take 10,000 people who are having hip replacement and they all followed this regime. With haemophilia you're lucky if you have a clinical trial with 100 people in it. That would be a large trial, but in statistical terms it's small.

So many of these trials were really small, and so I wouldn't be overly critical that this is the first guidance because, to be honest, this therapeutic landscape had really only just emerged.

Q. This document deprecates the absence of guidance from what's loosely described as regulatory authorities, and certainly it could be said that the picture that

emerges from the first half of the eighties is of clinicians having to take their own decisions about how to respond of risks, whether it be of hepatitis or HIV.

Do you think it would have been helpful for there to have been some form of central guidance, whether from the Department of Health or the Chief Medical Officer or some other authority or agent, rather than clinicians in the hundred or so Centres across the countries being left to make up their own mind?

A. Yes, I think it would have been helpful.

Q. Some of the documents that we've seen, and you've touched on it in your statement, refer to a debate about the use of high-purity products and the availability of funding for such products. I'm not going to go to any of the documents in relation to that, but could you just briefly outline for us what the situation was in relation to so-called high-purity products and what the difficulty was in terms of securing funding.

A. Well, in the early days of HIV, when we didn't have a test for HIV, patients were being monitored clinically, because it's a clinical diagnosis. But in the laboratory there were one or two surrogate tests you could do. You could test their CD4 count, the

T-helper cells, and the lymphocyte count and the blood count in general.

Now, when a test emerged, it became obvious that some of those patients that we'd been monitoring in this way, not knowing whether they had been infected with the AIDS virus or not, nevertheless had a low CD4 count. And so there's a lot of debate about that, and I published the odd paper about it. And it was concluded that it was probable that there were contaminants in the concentrate, maybe immunoglobulin, perhaps other growth factors, that interfered with the immune system in a non-specific way.

So when higher-purity products came along, they noticed that they didn't seem to cause this problem. The higher-purity products were developed partly because we wanted the product to be as pure as possible anyway. If you looked at an old-fashioned bottle of Factor VIII from the days of intermediate purity, there would be a bottle about this size, with 250 units in, a great big cake of protein at the bottom, and if you were able to take out all the spare bits that you didn't want, it would look like an empty bottle. The Factor VIII in that was just a trace. All the rest was fibrinogen and immunoglobulin and goodness knows what else.

And the high purity was developed partly because we

wanted purer products, but also because they realised that one of the problems heat treating and so on was it was a low-purity product. And if you had a higher-purity product, you could virologically treat it more aggressively. So that's why it was developed.

But then with all this background of immunological abnormalities in people who didn't have HIV, we began to wonder whether it would make a difference to the progress of HIV. And there were one or two studies that were done that suggested that patients treated with high purity Factor VIII progressed in their HIV more slowly, and so that was the bigger rationale.

There were a number of reasons for wanting to adopt these products. We suspected that they might be virologically safer. They were certainly easier for the patients to use, being higher purity, smaller volume, quicker to dissolve, the patients liked them. And finally, they might have clinical benefits for people with HIV. So I certainly canvassed for that.

Q. And I think you did introduce or you were able to introduce high-purity products at some stage when you were in Liverpool?

A. Yes, yes. I was able to do that quite quickly. There was very little resistance from the commissioners. The difficulty was I think the first product that came

on the market was Monoclate and Mononine from Armour.

One other thing they did at the same time, which is of interest I think to the Inquiry, was that they obtained the plasma only from the American Midwest. They stopped obtaining plasma from California and New York because those were HIV epicentres.

The equivalent in the UK would have been if they'd stopped obtaining plasma from London, but I don't think that was ever very actively discussed anyway. Yes, so, I managed to get them. And when I moved to Manchester, we switched over very quickly.

Q. And without going into the detail of what we see in a number of the documents, some Centres had great difficulty, it seems to be suggested, in obtaining the necessary funding to use high-purity products or to do so as quickly as they would like.

A. Yes, that's right. I think the difficulty is that, to be honest with you, the evidence that influenced the rate of progression of HIV was not strong. Some of the evidence, if you'd taken it to its logical extreme, would have implied that we should give this high-purity Factor VIII concentrate to people who had acquired HIV in other ways and who didn't even have haemophilia because they seemed to progress more slowly than any other group.

Q. In terms of hepatitis B, to what extent at Sheffield, Liverpool, or Manchester, did you encounter patients who had hepatitis B and required treatment?

A. Well, in all of those Centres, we had a handful of chronic carriers. I actually needle stuck myself from one of them and had to have immunoglobulin. There were not many because although a high proportion of the patients, particularly with severe haemophilia, had been exposed to hepatitis B through their concentrate -- I think in my report, I quote the figures from my MD thesis where I found that 80% of the patients in Sheffield with severe haemophilia had been exposed to hepatitis B, and 40% of the non-severe patients.

But fortunately, with hepatitis B, the chronic carrier rate is quite low. Only 5 to 10% become chronic carriers. Most get over their infection and it resolves, and it's only the chronic carriers who have the propensity to develop chronic liver disease.

Q. And did you have responsibility for the care of any patients who did develop chronic liver disease as a result of hepatitis B?

A. Yes. At least one of them underwent liver transplantation in Manchester. Treatment -- we used interferon and various other agents with hepatitis B

started probably earlier than with non-A, non-B hepatitis. But I referred all of those patients to the hepatologist because the treatment was different, and there was never likely to develop much experience in hepatitis B therapy.

Q. And to what extent did you encounter, again, whether at Sheffield, Liverpool or Manchester, cases of patients being infected with parvovirus?

A. Well, parvovirus is a common childhood illness, and I don't recall any of my patients developing it, though it's possible I might have missed it. Some of the reports, there must have been active surveillance going on because the patients were asymptomatic.

90% of the adult population have already been exposed to parvovirus. It causes fifth disease, characterised by the classic slapped face rash, I remember I got it along with my two children when I was already a senior lecturer. It can be a nasty illness if you get it in adulthood because you can get transient arthropathy.

The significance of this in the haemophilia story is that parvovirus is a protein-coated virus, and it's relatively resistant to viral attenuation techniques, and so those isolated outbreaks of parvovirus are clinically unimportant, but they illustrate the

limitations of the viral attenuation techniques, and this, along with various other agents like prions, are also extremely resistant to viral attenuation. It's probably impossible. These sort of things form a cornerstone of the argument for recombinant Factor VIII.

MS RICHARDS: Which is going to be my next topic, professor, but I note the time, sir, and wonder whether this would be a convenient moment for the afternoon break?

SIR BRIAN LANGSTAFF: Yes, it would. We'll take a break now, until 20 to four. So 20 to four.

(3.09 pm)

(A short break)

(3.38 pm)

MS RICHARDS: Professor Hay, I'm going to ask you about the issue of recombinant next. And I'm going to ask you to assist us with an overview of -- a chronological overview of the attempt to obtain funding for recombinants and the various impediments and how it was ultimately resolved.

I think if we could pick it up in this way: what was the first point at which recombinants became available for use in clinical trials?

A. Well, I used it in clinical trials both in Liverpool

and in Manchester. Those were Phase III clinical trials, so there would have been Phase I and Phase II before then. And that would have been 1993 and '94 and '95.

The advantage of Phase III is they need larger numbers, and it was the only way the patients could get access to recombinant. And the general agreement was that they would be allowed to continue on a trial product until it got licence, but then the difficulty was nobody would pay for it.

Q. And we've certainly come across experiences in other centres with patients who were part of that trial and receiving recombinants and then, because of the absence of funding, were expected to revert back to plasma-based concentrates. Is that what happened with your patients as well?

A. Yes, yes. And that's an unusual situation because the company, I think probably reasonably, won't continue to provide it for nothing once it's a fully licensed product, but they will continue to supply, even though the trial has finished, until it's fully licensed. So in some cases, the patients would have been treated with recombinant Factor VIII for maybe two or three years, and then all of a sudden they're in a position where they have to go back to the old stuff

for financial reasons.

Q. Then 1996, it became the policy of UKHCDO to recommend recombinant for all; is that right?

A. That's correct.

Q. And I don't think we need to go to it, but that was the recommendation in the later iteration of the guidance that we looked at earlier this afternoon.

A. Yes, it was. Although we announced the policy before we published the guidance.

Q. Although that was the recommendation, funding was not available for recombinant.

A. Yes.

Q. What steps were then taken to your knowledge to try and obtain funding for recombinant?

A. Well, we had negotiations with the companies to ask them to reduce their price, which didn't go very far. We spoke to the Department of Health, and a meeting was organised between the Haemophilia Society, myself, Professor Hill and Lord Hunt, who was the junior minister with responsibility for our clinical area at the time, to make representations to him. The patients campaigned very actively, to the extent that I remember parents chaining themselves to the railings of the Children's Hospital at one point. You can imagine the parents were particularly keen.

Understandable.

I think -- well, the difficulty was the Department of Health wouldn't accept the viral safety argument. We were arguing that given everything that had happened in the past with various viral agents that, by the time they were recognised, it was too late, that we wanted to give the patients the benefit of the doubt. There had been several episodes of odd infections here or there that had shown that the viral attenuation techniques, whilst very effective were not completely effective, and we were worried that some new agent might come along.

Q. And I think the way you've put it in your statement is that UKHCDO argued there'd been an outbreak of hepatitis A, that there was evidence of parvovirus transmission, and there were concerns about prions, and that there may be other unknown pathogens resistant to heat treatment.

A. Yes. The physical treatment required to inactivate prions would completely denature Factor VIII. So it's theoretically more or less impossible to attenuate that.

Q. There came a point when the Department of Health agreed to fund recombinant for patients under 18; is that correct?

A. That's correct. Though, interestingly, they did not

-- they still didn't concede the viral safety argument. They said that they were only doing this to allay the concerns of the parents, so that allowed them to climb down in a limited way whilst still not changing the argument. And so, under the age of 18, by the time the next stage came along, those 18-year-olds were in their early 20s.

Q. And that was, I think, 1998, and there was now recombinant Factor IX available, so children with haemophilia A and haemophilia B were able to access recombinant from around 1998 onwards.

A. That's right.

Q. There was an issue that arose, I don't know whether you can assist us with this, about non-availability of recombinant because of shortages of supply due, I think, to circumstances in a manufacturing plant in the States. Can you recall when that was?

A. Yes, I can. I mean, firstly, it's worth remembering, because it speaks to the issue of the adequacy of supply, that when the children went on to recombinant in 1998, we were unable to do it fully for a period of six months because it took that long for the manufacturers to wind up the supply to this country, because any supply that we were getting was in competition with other countries. And one of the

problems that we've had negotiating lower prices until relatively recently has been that it's been a suppliers' market. There has been a shortage of manufacturing capacity. That's no longer the case, but it was the case for quite a long while.

Now, I think the specific episode that you're referring to is the recombinant shortage starting, I think, about 2001 and lasting for two years when Bayer had an inspection of their Berkeley plant in California and their paperwork was not adequate. There was no suggestion that the product was unsafe. But whilst they sorted out their auditing processes, they were not allowed to issue a new product. Because a product licence is not just licensing the end product. You also licence the process which is then set in tablets of stone, and that process involves, amongst other things, auditing each step of the process, and that's where they were a little lacking.

So this was a huge problem because at that time the only suppliers were Baxter and Bayer and Wyeth, who were marketing ReFacto at that time, and so the supply of recombinant Factor VIII effectively halved to the whole world overnight. And this, amongst other things, is a reflection of why so many of us have a policy of not putting all our eggs in one basket, because there were

some Centres that only used Kogenate which was that Bayer product, so their supply wasn't cut in half overnight; they had no supply at all.

And the other manufacturers would naturally favour their existing customers. So I, as Vice-Chairman of UKHCDO, organised a system of supply swaps which had to be agreed with both the clinician and the supplier, who would often have an existing contract, so that we could shift supply from one Centre to another, to at least enable the younger children to remain on the recombinant. Because, otherwise, you would have had the situation where you'd have whole Centres where all of their kids would have had to go back to plasma derived. It was a compromise, obviously. One would have preferred to have kept all of them on recombinant, with that supplier. And we also negotiated as fast as we could for the other suppliers to increase their supply.

Q. Did it follow, however, that there were children, and probably in particular older children, for whom recombinant was no longer available and they had to revert to using plasma-based products?

A. They would have been predominantly older children.

Q. Now, your statement explains that in 2003, the Department of Health finally decided to make available funding for patients to switch to -- now adult

patients to switch to recombinant products; is that right?

A. That's correct.

Q. And what, if any, sense did you have in your capacity as Vice Chair of UKHCDO, of the reason for the Department's decision at that stage?

A. Well, we were all a bit puzzled. I don't know why it happened at that point, to be honest, because nothing much had changed. We were just very grateful, though with slightly mixed feelings because, as you know and I guess we're going to talk about it, the funding for that was staged.

Q. Yes. Can you explain what the situation was, then, in terms of the staging and the judgments that had to be made?

A. Off the top of my head, I can't remember the amounts. But in the final year, 44,000 -- sorry, £44 million was required. The problem financially, to put it into context, was that recombinant Factor VIII being recombinant attracted 20% VAT, whereas through some tax anomaly, plasma products are VAT exempt. And the unit price was twice as high, so recombinant products were very much more expensive than the plasma derived ones. So we needed a financial uplift to be able to change it.

Now, unfortunately, they staged a payment over three years, and it was very much backloaded. So I think there was something like 15 million made available in the first year, 22 million in the second. The figures may be wrong but the order of magnitude is about right.

And we had to devise a system to prioritise the patients. But, of course, naturally that gave rise to trouble. Because we and the Department of Health, you know, we'd have preferred not to have been in that position. We would have much preferred to have switched all the patients at once. But the Birchgrove Group, I think it was, objected to us prioritising younger patients, and they felt that those patients with HIV should start on recombinant first. We felt that the patients least likely to have been exposed to viruses should logically start first, and that was the Department of Health view. And so we segregated according to age.

Q. And how long did it take, then, for recombinant to be available to all patients who wanted it, but by what year was that process complete?

A. By 2006.

Q. And you've said in your statement that towards the end of the recombinant roll-out to adults, it became

apparent that funding might not be secure. What can you recall about that?

A. Well, what I think we were told was that the funding was separate; it was a separate uplift. We negotiated special contracts with all the suppliers that actually reduced the unit price and enabled us to roll things out slightly quicker. It was a very complex process. But towards the end, the Department of Health indicated to us that the money was going to be handed over to regional and district Health Authorities but that it might be bundled with other items of spending.

Now, the problem with bundling is that they might take three separate items of expenditure each costing, say, 10 million, and tell people to buy all that with 25 million. It's often a mechanism for actually cutting the funding. And we were very worried that that would cause us to have to revert to plasma derived which would have caused a storm of protest from everybody, not least the medical profession.

Q. You were asked in your statement the question, "Should recombinant blood products have been made available to all earlier than they were, and if so when?"

I'm just going to read out your answer and see if you have anything to add. You said in your statement:

"Yes. It was UKHCDO policy that we wished to treat

all our patients with recombinant Factor VIII from 1996 and for haemophilia B from 1998, when recombinant Factor VIII and then recombinant Factor IX became available. We wanted to give the patients the benefit of the doubt about safety based on the unknown virus hypothesis. Having been at least thrice bitten by previously unknown viral pathogens and knowing that some pathogens were difficult (protein-coated viruses such as parvovirus and HAV) or impossible (prions, the cause of vCJD and classical CJD) to inactivate, we wish to treat the patients with a product that should theoretically be free from all human pathogens."

Is that right, and is there anything that you would add to that?

A. The only thing I would add to that was, whilst you're reading it out it occurred to me that, actually, I think prions were the final nail in the coffin, as far as the Department of Health's argument that we should not change over to recombinant, because there could be no certainty about the clinical significance of variant Creutzfeldt-Jacob disease at that point in time.

Q. You've also said in your statement that the department's position which you described -- in other words, that they didn't accept that recombinant

Factor VIII or IX was not safer than plasma derived Factor VIII or IX -- has never changed to your knowledge; is that right?

A. Well, as far as I'm aware, that's the case.

Q. Professor Hay, that leads us on to vCJD. There are quite a few documents I might need to ask you to look at.

I'm going to start, sir, with a couple and then perhaps leave the rest until tomorrow morning.

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: So, in terms of the vCJD notification process, I just wanted to start in 1997 with -- I think this is the right reference, Soumik -- HSOC0015148.

Yes, I think I might have put in an extra digit. HSOC0015148.

So this is a letter dated 26 November 1997. It's co-authored by you, and it reads as a letter sent to patients. You say:

"I'm writing to you following the recent Panorama programme and in anticipation of further press reports to outline the current situation in relation to this condition [ie new variant CJD]. I would also like to keep you informed of the measures which we've decided to take at the Manchester Haemophilia Centre and the

reasons for these."

You then talk in the next paragraph about what CJD is, and the infective agent being thought to be a prion. You say in the last two sentences of that paragraph:

"There is no evidence that CJD can be transmitted by blood or blood products. Furthermore, there have been no reports of classical CJD in patients requiring regular blood transfusion or in patients with haemophilia."

If we then go over the page, second paragraph, you then talk about new variant CJD. You explain it's different from classical CJD, appears to affect young people, and you describe how it's caused.

And then in the next paragraph, you go on to say that:

"There's a very small theoretical possibility that new variant CJD might be transmitted by blood transfusion, although experience would suggest that only a small number of susceptible individuals would be at risk. In light of this, the Government has been advised to consider the possibility of filtering out all the white cells from whole blood and is currently commissioning an independent risk assessment which will take six months to report.

"Three weeks ago, BPL withdrew a batch of 8Y

Factor VIII concentrate because two of the donors had developed new variant CJD. Neither of the Manchester Haemophilia Centres have used these batches."

Then you say this:

"Last week, the executive committee of the UK Haemophilia Centre Directors met with experts in CJD and plasma fractionation to consider the problem. Blood products like Factor VIII are already made from plasma with white cells removed and do not transmit infections associated with white cells like glandular fever or cytomegalovirus and may not therefore transmit new variant CJD."

Then you talk about the possibility of inactivation.

Then this:

"The Haemophilia Centre Directors concluded that there was most likely to be little or no risk of infection with [new variant] CJD from blood products. Since there can be no absolute certainty about this for some time it was felt that until the results of the DOH risk-assessment were known, that blood products of UK origin should be temporarily phased out. In their place, products manufactured from plasma taken from areas free from BSE and [new variant] CJD such as the USA will be used. There are currently inadequate supplies of these American products in the UK and so we

plan to replace Replinate and Replinine with alternative products as stocks run out."

Then you offer patients the opportunity to call the Centre and then you say you've arranged for a meeting at the main lecture centre at the Manchester Royal Infirmary on 11th December "to present the evidence and discuss the matter, to which you are invited".

Was this, in 1997, the first main action taken by UKHCDO and then directors such as yourself in response to the developing knowledge about new variant CJD?

A. Yes.

Q. Did the meeting you've described in that last paragraph take place?

A. Yes.

Q. And what can you tell us about that meeting?

A. To be honest I can't remember that meeting but it certainly took place. I think it was well attended, and we would have had a question and answer session. I would have made a presentation about what we did and did not know.

Q. Can you recall what the reaction of patients was to news of a further potential threat to their wellbeing, and the news that there was going to be a reversion from UK-sourced blood products to US-sourced blood products, in some respects, the reverse of what had

previously happened. How did patients respond to that?

A. Well, as you might imagine, their responses were very varied. We always -- well, we knew, because of the way that prions work, that only perhaps a third of the patients would be susceptible. Those are the ones who are homozygotes. And so -- of course, we didn't know who was homozygous or heterozygous, but we did know that it was unlikely that it would be like hepatitis C or HIV and infect people indiscriminately. There were theoretical reasons for thinking that in this particular instance, the risk of transmission by clotting factor concentrates would be low. But having learned from past experience, I felt that it was important to emphasise what we did not know. Patients understand that. And in my experience it's much better to say, "You know, this is not known, it may take years to know", than to offer them some sort of speculation that they may take away as hard and fast fact which might turn out to be untrue.

I go into my -- in my report I go into the reasons why we felt that concentrates would be much less likely to transmit this agent than a whole unit of blood. And I would describe that to patients, but I would also say, "You know, we'll just have to keep an eye on everybody

that has had these products, because there may be no certainty about any of this for maybe ten or 20 years."

And some of the patients got very distressed. Others were quite philosophical, and probably went away with the relative reassurance that they'd been provided. At the end of the day at this point we didn't even have any evidence that variant Jakob-Creutzfeldt Disease could be transmitted by blood, let alone the other products. This was in relation to discovering variant Jakob-Creutzfeldt Disease in donors of blood and the recognition that, histologically, one of the ways in which variant Jakob-Creutzfeldt Disease differed from classical Jakob-Creutzfeldt Disease is that you could demonstrate the prion protein in the lymph nodes and in lymphocytes, which are obviously elements of the blood system, whereas classical Jakob-Creutzfeldt disease is found in the central nervous system and you don't find it elsewhere. So that raised, at quite an early stage in our knowledge of the condition, the theoretical possibility that it could be transmitted by certainly whole blood, less certainly plasma.

Q. This letter refers to the UKHCDO Directors Executive Committee having met with experts in CJD and plasma fractionation. At this stage, was there any particular involvement or direct involvement from the

Department of Health in those deliberations?
A. I don't remember so -- but they were certainly very much involved from an early stage thereafter.
Q. I want to pick up a document trail from 2004 onwards with you, and I'll do that tomorrow morning, because there are then a range of notifications from 2004 onwards with which you were closely involved in your capacity as vice chair and then chair of UKHCDO.
But before we do that, can you recall, for after 1997 and prior to 2004, what further processes there were involving patients and providing information to patients?
A. Well, the reason for doing this by letter, and then following up with a meeting rather than to do it individually, was because the press were finding out about it, and we needed to get to speak to the patients as quickly as we possibly could. As many of the consequent conversations as possible were done on an individual basis, mostly in clinic but sometimes in the Centre.
Many of these conversations were quite protracted because some of the concepts involved, for example the concept of the public health risk, were very difficult for doctors to understand, let alone laypeople. And I think caused a lot of confusion. So, yeah.

MS RICHARDS: Sir, I'm conscious of the time. There are quite a few documents I think it will be useful to look at with Professor Hay on the CJD notification process from the UKHCDO perspective, but it might be more sensible to pick those up in the morning.
SIR BRIAN LANGSTAFF: Well, I think it's important evidence. It's late-ish in the day. I'm sure, professor, you've had a longish day. Can we meet again at ten o'clock in the morning?
THE WITNESS: Sure. Certainly.
SIR BRIAN LANGSTAFF: And the same rules apply as applied at every break during the day, but have a good evening and stay safe, and the same to everyone else.
I look forward to meeting you, Ms Richards, tomorrow at ten. You heard what I had to say earlier this week about the attendance of others at the hearing centre following what I imagine will be the acceptance of Parliament of the Government's proposals today about coronavirus.
Thank you very much.
MS RICHARDS: Thank you, sir.
THE WITNESS: Thank you.
(4.08 pm)
(The hearing adjourned until 10.00 am the following day)

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