Tuesday, 6 October 2020

(10.00 am)

SIR BRIAN LANGSTAFF: Today we have Dr Colvin.

MS RICHARDS: We do, sir.

SIR BRIAN LANGSTAFF: Dr Colvin, may he be sworn.

DR BRIAN TREVOR COLVIN (sworn)

Questioned by MS RICHARDS

Q. Dr Colvin, you provided a detailed CV to the Inquiry along with your statement. I'll just go through some of the elements of your career most relevant to the Inquiry's investigation.

You undertook your medical training at what was then known as The London Hospital. When did it become The Royal London Hospital?

A. It became The Royal London when the Queen came to see us on our 250th anniversary. The hospital was founded in 1740, so 1990 was the 250th anniversary.

Q. So you were trained there. Then you worked as a junior doctor there from 1969 to 1975, I think, in general medicine, cardiology, and then haematology?

A. Yes. I was a junior doctor really up to 1977, when I was appointed a senior lecturer and honorary consultant at The London. So my general training was up to about '73 or '74, but I became a consultant in '77.

Q. What did the haematology training, the specialist haematology training, comprise prior to your appointment as a consultant?

A. It comprised mostly what can only be described as an apprenticeship. There were one or two lectures that took place at the Hammersmith. There was really no formal training. I think it was to do with apprenticeship and reading.

Q. In terms of training in relation to matters relevant to the care of patients with bleeding disorders, was that something that you did during this time under Professor Jenkins?

A. Yes, indeed. I might just make a brief point, perhaps, about what Mark Winter said last week.

I began my training in '69/'70 with the absolute intention of being a physician as well as a pathologist. So although Mark was saying that he was the first generation of people who were physicians and pathologists, I'd like to claim four years earlier. That's exactly what I wanted to do, and he was quite right to emphasise it.

Q. So would you accept, whatever the precise timing, the broad point he was making, that there may be a difference between those whose path to specialising in the care of patients with haemophilia was

a laboratory-based path, scientific path, and those whose path was through general medicine?

A. Yes, if you look at the content of the so-called Reference Directors in the time that I was about to qualify in haematology, some were physicians, not haematologists; some were haematologists who were clinical haematologists; some were haematologists who were laboratory haematologists, and we had one paediatrician. There was a number of different ways of being a Haemophilia Centre Director. I think the fact that juniors like myself or like Mark became members of the Royal College of Physicians and of the Royal College of Pathologists was key in our desire to be physicians and pathologists, and I think this will come out quite a bit later.

Q. Then your post as a lecturer in haematology, which I think your CV identifies as being from 1975 to 1977, what did that comprise?

A. Well, really it was being a senior registrar, to be honest. It happened at the London Hospital Medical College that all appointments in pathology were academic. But you will have seen from my CV that I was never primarily academic. I was primarily a physician and pathologist.

Q. You refer in your statement to having undergone some

training in blood transfusion at the Brentwood Regional Transfusion Centre. What did that comprise?

A. This was absolutely obligatory for -- and I've said that the training programme was an apprenticeship, and it was an apprenticeship, but part of that apprenticeship was to be seconded to the Brentwood Blood Transfusion Service. There, one was introduced to aspects like fractionation, blood cross-matching, nitrogen frozen blood (which happened to be a particular feature of Brentwood), and the general practice not only of blood transfusion in its administration but in really practical matters.

I mean, when I qualified in '69 and then was in the laboratories in 1970, I would actually do all the blood tests for the entire hospital during the night without any training in haematology, chemistry and microbiology in a way which is unthinkable, thank goodness, today. Even into my time when I was a consultant, I was still capable of performing Factor VIII assays with my bare hands in the middle of the night which nobody would think of doing today.

Q. You then took up your consultant post in 1977 at The London Hospital, and you became effectively the consultant responsible for the haemophilia service there, albeit I think Professor Jenkins remained the

nominal director until the mid-'80s?
A. Yes. I mean, George (who is still alive in his 90s) was the consultant haematologist and the director of the non-haemophilia centre, and we had a physician called Dr Adam Turnbull, who is unfortunately deceased. George and Adam together, really as a physician and as a pathologist, were in charge of haematology, but Frank Boulton, who actually has been referred to in this Inquiry, was going to look after haemophilia, but he then left after a year or two of being in post. That was my opportunity to be promoted to the position of senior lecturer, and that was when I was given the task of, if you like, looking after people with haemophilia and building a haemophilia centre.
Q. Then you remained a consultant and director of the haemophilia service until your retirement in 2007?
A. Yes.
Q. I think you carried on with some clinical responsibilities until 2009?
A. All that happened was when I retired, John Pasi (who is now director of the centre) was appointed in 2003 really as a kind of preparatory to my retirement, I suppose. When I retired in April 2007, there was a great shortage of clinicians to do the work, and

I was asked if I would come back to do one session a week in the clinic without any administrative responsibilities. At that time, I was still digging for students at the London Hospital Medical College because, although I had retired, my senior colleague the warden had asked me not to leave my post as Dean for student affairs. So I continued for a year until -- two years really -- doing one clinic a week just sitting in the clinic until, in 2009, I retired completely from clinical practice.
Q. Between 1997 and 2007, you were chair of the Clinical Ethics Committee at the Barts and London NHS Trust which was what the trust was now known as. What did that entail?
A. Well, Len Doyle was an American ethicist who decided that it would be a good idea to have a clinical, as opposed to research, ethics committee. My mentor, Dr Alistair MacDonald, was Chairman of that committee until he retired, and then I was persuaded by Len, who was a very good friend of mine -- and he will also appear later in these discussions, I think -- he persuaded me to take the chair of the committee, and the committee was there to address difficulties of a clinical nature in an ethical context.
I mean, for instance, we designed the consent

form for the hospital. We addressed issues like whether it was possible for unconscious patients in great difficulty to really be offered research projects which definitely needed to be done by somebody, and whether it was possible for anybody to give valid consent in an Emergency Department for, for instance, some kind of clot-busting procedure when you had a heart attack. I'm just giving an example, but there were a number of issues like that.
Occasionally, there were ethical issues which were to do with individual patients and, occasionally, somebody would come to me or to Len and say, "I've got this really difficult problem. Could you come up to the ward and have a look at what's happening?" Then Len and I would discuss together and would try to reach an advisory conclusion as to what should be done in a particular difficult position.
Q. That's distinct from the role a research ethics committee which has a much more structured remit and process.
A. A completely different function, and I think it's very important to draw that distinction. I think that when we started not many hospitals had clinical ethics committees and I think that it was an American concept. I think it was because Len was an American

that he brought in the Clinical Ethics Committee idea so early to the London. Whether there is still a Clinical Ethics Committee, I wouldn't know.
Q. Did that ethics committee exist prior to 1997, or was that when it was --
A. Yes, because I think Alistair MacDonald was Chairman before me, so, yes, I think it must have done.
Q. Do you have any idea as to when it first --
A. No, I don't know when it was founded, although I imagine that could be discovered, but I don't know.
Q. Then you were chair of the Ethics Committee of the Royal College of Pathologists between 2003 and 2008. What did that entail?
A. Well, when -- I think the College of Pathologists realised that there was all sorts of areas of importance in pathology which needed to be thought about in an ethical framework, and there was also a need for a lay adviser for the college in this context. So I was asked by the then president if I would form a clinical ethics committee to look at pathology, procedure and ethics, and we did. We published one or two leaflets, and we tried to bring the idea of ethics into pathology.
I'm not sure how much real business that we were able to do in the period that I was actually Chair,

but we certainly created the Ethics Committee, which continues to the present day, and it certainly had a strong lay influence to make sure that lay people had the opportunity to advise the Royal College.

Q. You had a role with the Safety Committee of the Scottish National Blood Transfusion Service. Henry, could we just have up on screen, please, GRAM0000006_002, please.

So we can see here it's referred to as the Scottish National Blood Transfusion Service Factor VIII and Factor IX Safety Committee. This is a draft remit. The tasks are there set out:

"Reviewing clinical trial protocols, reviewing data generated in the course of clinical trials, reviewing serious adverse events, reviewing unexpected or ambiguous events, commenting on trends identified during clinical trials, commenting on interim analyses of clinical trial data, and then providing similar services in respect of post-marketing surveillance studies and general pharmacovigilance."

What was the nature of the committee, and when were you on it?

A. I was asked by Professor Ludlam if I would be willing to chair this committee and was flown up, at very short notice actually, to Edinburgh to, I think, its

first meeting. I'm not sure that it ever actually did anything very much because I can't recall making a significant contribution. You'd need to remind me the exact year that I was Chairman.

Q. I was hoping you would be able to tell me that --

A. I can't remember, but it was quite late in the day and I don't recall our making a significant contribution because I think that the Safety Committee was founded when essentially most of the problems had already been dealt with.

Q. During your time as consultant at The Royal London and director of the service, you were a member of UKHCDO. We'll come on in more detail to UKHCDO's role, but I think you attended your first AGM in 1977, having taken over the service at the Royal London?

A. Yes.

Q. You were Chair of UKHCDO between October 1993 and October 1996?

A. Correct.

Q. You were not, during the '70s and '80s, a Reference Centre Director?

A. Perhaps I should explain that for you. When I started my work in haemophilia, which I suppose was probably 1975 -- I still have on my desk a little marble paperweight of the meeting in '75 in London. I can

remember actually seeing the parents of one of my patients in '75 at that meeting. So I was clearly involved in haemophilia care as early as '75. But I've explained that the haemophilia centre in '75 really didn't exist. The first thing we did, I think, was for me to go over to the Royal Free Hospital to see the late Katharine Dormandy, who was actually on her death bed at the time -- I went to her home -- and decided what we could do about haemophilia in North East Thames region in addition to the great work that the Royal Free were doing.

So, at a national level -- I'm sorry, I'm diverging slightly -- but on a national level, I had no status whatsoever; I was just a minnow in the haemophilia care system. So I would be invited to meetings or the annual meeting of Haemophilia Centre Directors, but my influence was zero and, indeed, that influence remained at zero until 1993 when I was called on the telephone -- I can remember the conversation now. Dr Rizza phoned me and said, "Brian, would you like to take over the chair of UKHCDO?" Which was a very great surprise to me.

Why that happened I think you would have to ask other people. But it was right at the time when we were trying to improve the management of UKHCDO in

a number of different ways, which we may, I guess, come on to, and I think there was a feeling -- maybe there was a feeling. Once again, I think you would have to ask others. But maybe there was a feeling they needed a new-ish broom to look at what UKHCDO was doing in an independent way, and so I found myself suddenly, having been nobody, chairing the organisation.

Q. We will come back later in a little more detail to UKHCDO's role.

You were also a member, and you touched on it a moment ago, of the North East Thames Region Association of Haematologists, and we're going to look at some of the documents generated by that, so I'll ask you more about that in due course.

You were a member of the Medical Advisory Panel of The Haemophilia Society.

A. Well, I began to be involved with Haemophilia Society really quite early on, and I think I referred in my statement to one or two meetings where I gave talks. I can remember on one occasion taking part in a debate at The Haemophilia Society at one of their weekends, "I have the right to go skiing", and made a presentation about it.

So I used to support The Haemophilia Society.

They used to ask me to do things. But I was never really aware of the time when I ceased to be the medical adviser. I think that they didn't ask me after a while to do any more for whatever reason, but they never wrote to me saying, "You're not a medical adviser anymore."

Q. Then you're -- lastly, by way of introduction, you gave evidence to the Lindsay Tribunal in Ireland, the Archer Inquiry, and the Penrose Inquiry in Scotland.

A. So I gave evidence at the Lindsay Inquiry I think largely because a friend of mine had a relative who was a haematologist in the Republic, and I think I was asked to go to the Lindsay Inquiry to support her. I know she's deceased now, so I can't give you any detail. I just think it was through that route that I was asked to go to Lindsay through the route of somebody who was practising haematology in Ireland at the time.

Q. Would that have been Dr Daly?

A. No, it wasn't. I can tell you who it was if you need to know.

Q. Unless it's a UK-based haematologist, we don't particularly need to know.

A. Okay. My presence at the Archer Inquiry was entirely determined by the late Reverend Alan Tanner. Alan

rang me up during the Inquiry and said, "Brian, would you be willing to attend the House of Lords to give evidence yourself because we would like you to do so." That's another example, really, where I always tried to help society, and certainly Alan Tanner, whenever I could because I had a huge respect and affection for him, and when he asked me to do this, I willingly did so.

I think my relation with the Penrose inquiry is, I think, probably rather more formal.

Q. In relation to the Penrose Inquiry, you were asked to address two particular issues. One was the care of one of the deceased individuals who the Penrose Inquiry was considering, and the other was an issue about whether certain products should have been available in Scotland between 1985 and 1987.

You didn't give wider evidence I think to the Penrose Inquiry?

A. No. I think I actually gave what was effectively medico-legal evidence on two or three patients, rather than just one, but there were these two separate issues: one, the medico-legal issue, if you like, in terms of looking at an individual person's course; and the other was, as you said, the issue of a particular concentrate.

Q. I understand from your statement that you were involved in relation to a number of legal claims brought against what then, I suspect, had been the health authority responsible for The London Hospital as part of the HIV litigation?

A. Well, in 1990, there were 30 lawsuits on my desk, and I think this was related -- perhaps it's not for me to judge -- but I think these were related to The Haemophilia Society's campaign for compensation or whatever you'd like to call it. Compensation is impossible for these circumstances, but some kind of financial recognition of what had happened.

So I began to look and to defend these cases with the Trust's solicitor, who happened to be the biggest Trust standard at the time. Then, of course, when John Major came to the premiership, he introduced what became the Macfarlane Trust, and the cases were dropped.

Q. I want to ask you a little more about the facilities and services at The London Hospital.

Could you start by describing what the staffing and facilities were in 1977 when you took up your consultant post.

A. So there is an 18th century hospital with a 19th century out-patients. There was no day ward. There

was nowhere to see patients other than really in my office, I think. There were -- there was a laboratory which I was certainly competent to do all the haemophilia tests personally. There was no nursing staff, no physiotherapy staff, no social work or counselling staff. We had cryoprecipitate and a little bit of NHS, and I think at that time even then commercial concentrate.

So if patients wanted to come to see me with haemophilia, or see the hospital with haemophilia, they would just simply turn up I think in the Emergency Department, and then somebody would go and see them and, if they needed treatment, we would treat them with cryoprecipitate. So I would get the cryoprecipitate out of the freezer, put it in the water bath for half an hour, draw it up myself into a horse syringe, or my junior staff would. I mean, there were certainly junior staff around. So the whole thing was done absolutely on a basis which is unthinkable today.

Q. We're going to look at a document from 1977, just to get a sense of the number of patients at that time and the geography of the area. Henry, it's HSOC0022537, please. This is a document authored by you, regional co-ordinator for haemophilia in domiciliary care --

sorry, co-authored by you, along with others including Professor Jenkins and Dr Katharine Dormandy published in the British Medical Journal in 1977.

We can see there reference to the North East Thames region -- and we'll look in a moment at what that comprised:

"Having appointed a nursing sister to co-ordinate the organisation of care for haemophiliacs in the region, and as a result of that, it's recorded that facilities for home treatment have expanded rapidly. Several associate centres providing care to haemophiliacs had been set up around the region, in addition to the four main haemophilia centres, which are all in the south-west corner of the region. As well as providing support and supervision of patients on home treatment, the co-ordinator helps to place haemophiliac children in suitable schools, maintains the regional register of haemophiliacs, and has a more general role in ensuring that services are available where they are needed throughout the region."

If you just go two pages further on, Henry, to page 3, we can see a map there. Could we just zoom in on the map, please? So this is the North East Thames region; is that right?

A. Yes. You'll also, I think, see on the left-hand side

a white area which is the old North East Metropolitan region. Now, this is very boring bureaucracy, but the Royal Free used to be in the old North East Metropolitan region, but I think was not in the North East Thames region. When I began my career, it was North East Metropolitan, which I think I actually -- perhaps it's the other way around. I'm sorry. I think may have misled you because it's actually on this slide that the Royal Free was not in the old North East Metropolitan region but was in the North East Thames region. I'm so sorry.

Q. That's all right. We see here the four main haemophilia centres there referred to are the Royal Free, University College Hospital, London Hospital, and the Hospital for Sick Children; that would be Great Ormond Street?

A. Yes.

Q. Then we can see there are then four -- these four associate centres at Harlow, Colchester, Chelmsford and Grays.

A. Yes.

Q. Then we see in the middle there the Brentwood Regional Transfusion Centre. Am I right in understanding that the Regional Transfusion Centre in Brentford*(sic)* was the supplier of NHS concentrates and cryoprecipitate

to all of these centres?

A. Brentwood. But, yes, absolutely. Obviously, it was geographically in the middle of the region, therefore quite well placed, geographically, to distribute the concentrate. But, of course, it was also in a rural area, so in some ways, that wasn't so convenient.

Q. We'll see in a little while when we look at some of the North East Thames Region Association meeting minutes how things were organised as between, in particular, The London Hospital and the Royal Free.

But just dealing with the associate centres for the moment because we may not hear evidence directly from consultants or doctors at those centres, what autonomy did those associate centres have?

A. I think they had complete autonomy if they cared to exercise it. I should add, perhaps, that Southend became very important later because we sent a consultant from the London who trained at the London down to Southend, and Southend became an important associate centre.

Q. Who was that doctor?

A. Dr Michael Mills went down to Southend. But I think the answer was that we regarded this as being completely shared care. So the consultants at these hospitals had autonomy. They asked for our advice and

our support, and the patients came to see us at the London or the Royal Free, but they were autonomous. Of course, the Royal Free had interests in north-west London as well as north-east London. But my perception, when I was appointed in '77, was that there was a real need in Whitechapel and in Essex for a proper haemophilia centre. This, of course, is the case that the Royal Free, who are a famous and brilliant haemophilia centre, originally admittedly started in a caravan, but it had become a really important and national leading centre. But geographically, it was in Belsize Park, and so for a patient to be looked after from Colchester going to Belsize Park, not a terribly easy journey. Of course, Whitechapel is also the extreme west of the area, but I think it had some strength in terms of transport links that the Royal Free didn't have.

I should also add that at that time Cambridge, for all its many strengths, was not particularly haemophilia orientated. So I think we tended to draw patients from the north-east of the region -- and you can see how wide that is on the map -- who might geographically naturally have gone to Cambridge but preferred in fact to come into London.

So when I was appointed, one of the first things

I did was to start outreach clinics. So I went out, actually with my wife, on a Saturday morning to places like Chelmsford and Colchester and Harlow to, if you like, fly the haemophilia flag, to say: look, we're trying to do better for people with haemophilia, we want to look after all your needs, we believe in the concept of, what later became, comprehensive care. There's the opportunity, perhaps for home treatment.

I would actually see patients in these hospitals on a Saturday morning, perhaps give a talk to the sort of, effectively, The Haemophilia Society community, and in that way we drew people in. We found all sorts of people with haemophilia who had not been looked after. I mean, there was one patient who, I suppose in his 60s when I first met him, literally had knees that were in fixed sections. All he could really do was to lie in bed, read The Times and watch the cricket on television. That was his life.

We tried to improve the lives of people who really didn't even know there was a haemophilia service.

Q. If we go over the page please, Henry, we can see a table -- if we zoom in on the second of the tables, please, Henry.

So we can see here this is obviously a snapshot

in 1977:

"Numbers of patients cared for at each centre and treated at home according to type of haemophilia and preparation."

We can see The London Hospital is considered as having three treated at home with Factor VIII cryoprecipitate, eight on Factor VIII concentrate (that's in terms of haemophilia A), and then (in terms of haemophilia B) two patients on home treatment with Factor IX concentrate. So a total at that stage of 13 patients on home treatment.

I think we see elsewhere -- oh, yes, if we just go up to the table above that, I think we've got a figure somewhere, I can't find it now, of the number of patients that were being treated under The London Hospital umbrella, as it were, and it was 190. I can find the reference to that if need be.

Just, again, a further snapshot in time, Dr Colvin, moving forward to 1983, could we have, Henry, BART0002284, please.

This is a document we may come back to, but we can see its co-authored between you and Dr Kernoff of the Royal Free in August 1983, "Haemophilia Services in the North East Thames Region".

If we could go, please, to the sixth page, we

can see there a description of The London Hospital. This is in 1983:

"The London Hospital Haemophilia Centre has its largest catchment area in East London, but also cares for patients throughout Essex."

And then:

"Both the [Royal Free] and [The London Hospital] Centres operate comprehensive care programmes for haemophiliacs which include genetic counselling, diagnostic services, paediatric and adult out-patient and in-patient clinical services, home treatment, physiotherapy, social services, general and orthopaedic surgery, dental surgery and emergency care."

Also reference to having:

"... the facility to patients with inhibitors and problems related to hepatitis."

We'll come back to hepatitis.

Then:

"UCH and the Middlesex ... [are] designated Haemophilia Centres but only care for small numbers of patients, and offer less comprehensive services."

So it would seem that in the six years from 1977 to 1983, the haemophilia service at The London Hospital changed and developed quite considerably?

A. I certainly hope so but I'm afraid that the fabric hadn't changed very much. I mean, I think that one of the features of haemophilic care is it's really the people rather than the fabric that make a haemophilia centre. I think the Royal Free were very fortunate that they had a purpose-built haemophilia centre about the time of Katharine Dormandy's retirement and sad death, but we didn't have that facility.

So there's no doubt that the fabric of the Royal Free was much, much more sophisticated than the fabric at the London.

As you will realise from my statement, I relied very heavily on the Royal Free for advice. I was a single-handed, effectively -- I know there are other consultants at the London but I was -- in terms of haemophilia care, I was single-handed. I have occasionally said, and I think it's fair, that I was on call from 1977 to 2003, when John Pasi became a consultant at The London.

But I relied on the Royal Free for my advice, and they were extremely supportive. That work we did in the North East Thames region I think was absolutely the right way to have managed haemophilia.

Of course you could have said, "Well, don't bother with The London, the Royal Free can do it all

themselves, and they could have done, but I do think that the people of Whitechapel and Essex benefited from having a significant centre at The London, although it wasn't the same as the centre at the Royal Free.

Q. If we just go further down the page, please, Henry, we can see it's said:

"There are Associate Haemophilia Centres at Chelmsford, Colchester, Harlow, Orsett and Southend."

So now Southend.

"These Centres do not separately register patients or organise home treatment programmes and are not staffed or equipped to manage serious clinical problems, undertake major surgery or offer genetic counselling. Their main role is to offer local support to patients who are mainly managed at the [Royal Free] or London Hospitals."

So, typically, if you had a patient whose local hospital was one of those five associate centres, what aspect of their clinical care would be your responsibility and what aspect would be the associate centres?

A. It would depend a bit on how severely affected they were. If they were severely affected, then I would hope that they would come to The London for regular

review, probably every three to 6 months, that we would advise them on all matters related to home therapy. You will see from the previous paper that you showed me that in '77 we appointed the domiciliary sister; and this was a key part of our outreach programme because she travelled all over the region looking at our patients in the home, helping them with their home treatment, advising them on how they were getting on, and whilst I said to you that in '77 the associate centres were autonomous, and indeed they were, because I couldn't force them to do anything, but they very willing and happily, I think, allowed or instructed or requested me to look after their patients but with total shared care.

I think it's terribly important that these patients were not lost to their distant -- for me, distant for me -- hospital. Because when things happen, you need to know where to go, what to do, and so it's no good having an ivory tower, if you like in -- no towers in Whitechapel are ivory -- but no point going to an ivory tower in Whitechapel when anything happens and you have to go to, say, Southend they don't know who you are. So the whole idea was shared -- shared -- care but we would be responsible for most supply, the home treatment programme,

prophylaxis when it happened in the 1990s, and things like genetic counselling when that became more important in later times.

So things that required what you might describe as critical mass or expertise we tried to deal with at The London or at the Royal Free but things that were everyday were happily dealt with at a place like Southend or Harlow, and I was determined that those associate centres should not lose touch with my patients.

Now, it was the case -- and this came up in the 90s when we were managing the definition and the accreditation of the comprehensive care centres -- what is the role of the associate centre? How do we police, if you like to use that word, the care provided in the periphery? It's extremely difficult. So it is a matter of personal relationships between the centre and the periphery to make sure that the patients get the expertise that's required at the hospital and yet they also have a contact with their local physician.

Q. If we leave this up, Henry, because I'm going to look at the bottom of the page in a moment -- but just so I understand the position in relation to the different centres and the way they interacted in the late 70s,

early 80s, there were essentially, is this right, three types of centre: the reference centres?

A. Yes.

Q. The main centres that were not reference centres, of which The London Hospital would be one, and then the associate centres?

A. Yes, that's perfectly correct.

Q. The status of reference centre was, at that time, was a DHSS conferred status; is that correct?

A. Well, it's probably more complicated than that. I think that in the 50s -- I don't want to go on too much, but in the 50s Macfarlane invented haemophilia care, really, for the United Kingdom, in Oxford. Then in the 60s I think half a dozen physicians, haematologists, got together, as part of the MRC I think, to create a system for managing haemophilia and, from that, grew UKHCDO.

Although I'm sure we will be discussing later some of the data aspects of UKHCDO, it was a world-class arrangement for managing the national care of people with haemophilia on the basis of the centres who were most interested in delivering healthcare. This group of reference centres were actually self-appointed, if you like, and they represented those cities that had the greatest

interest in haemophilia care.

Now, that meant that Sheffield was represented, but not Bristol; oxford had enormous influence over the whole of the middle of the country; nothing at Southampton, for instance; nothing at all in the West Country; manchester, yes; Birmingham, yes; Glasgow, yes; Edinburgh, yes; as I say, Sheffield; and of course St Thomas' and the Royal Free. But there was no sort of -- there was -- it's a brilliant organisation, but it was a self-invented organisation.

Q. Then we will just look at the numbers at the bottom of the page. So this, again, is a snapshot from 1983. We have there the figures of -- in terms of patients registered at The London Hospital: 201 with haemophilia A, 28 with haemophilia B, 109 with von Willebrand's, and then 36 patients on home treatment.

So you have gone from some 13 or so patients on home treatment in 1977 to 36 patients on home treatment by 1983?

A. I think it's important to appreciate that the Royal Free is actually bigger than this. I think that these figures may relate to the North West Thames -- it may not relate to the North West Thames -- influenced the Royal Free because the Royal Free has

enormous influence in North West Thames, which isn't actually, obviously, the North East Thames. We did have a north regional meeting from time to time but it's sometimes difficult to know whether the figures are actually all the Royal Free's figures or only some of them.

Q. I can clarify that with Professor Lee or Professor Tivnum in due course. But as far as your figures are concerned, this is a document authored by you in 1983, so it should be accurate?

A. Yes. Yes, of course. No, I've no problem with that.

Q. Without going to any further documents at the moment in relation to figures, your statement and I think your evidence to previous inquiries tells us, in terms of the growth of the centre, that by 1993 you thought you had around 500 patients, and by 2001 approximately 600 patients?

A. If that's what I said, yes, I'm sure it's fine.

Q. You say in relation to patients of that magnitude it would be about 100 that you would see regularly?

A. Yes. I mean, one of the features of my outreach programme was that I tripped over, if you like, a lot of people who were quite mildly affected and, as you'll appreciate, the numbers of people who have got severe haemophilia compared to the people who have got

haemophilia as a whole is, I don't know, perhaps 20 per cent or something like that. Those patients you will know about. But there are people out there who don't know they've got haemophilia and, if you have an outreach programme, you pick up people with very mild haemophilia.

So you might find that at The London after this outreach initiative we had rather more mildly affected patients on our books than other centres who hadn't been out looking for patients. As I think I've mentioned elsewhere, there are occasions when one can diagnose a patient with haemophilia at the age of 70. I've certainly done that a couple of times, where somebody's come to the hospital bleeding to death, say, from a prostate operation, and I've been able to identify they have got haemophilia, despite they've spent the whole of their lives not knowing that they had anything wrong with them.

Q. In 1993 The London Hospital became a comprehensive care centre. What did that mean?

A. Well, I think what actually happened was that they wanted to me to chair the organisation, and the only way I could be chairman of the organisation is if my centre was a comprehensive care centre. So I think on one day they decided I was a Reference Centre Director

effectively in order to get me into the organisation, and the only way to do that was to say I was a comprehensive care centre. I think I met the criteria but that's I think how it really happened.

Q. Before we look in a moment at more detail at issues relating to hepatitis, just one further question on organisation and administration.

Your statement refers to a system of red or brown envelopes.

A. Yes.

Q. What did that refer to?

A. Okay. So when I started at The London as the director, or indeed when I was a junior doctor, somebody -- I think John Perrin, who was the person who looked after the few haemophiliacs before -- or people with haemophilia -- before Frank Boulton, had started a system of identifying people with haemophilia and keeping a little folder, in a brown envelope, in the department that was separate from the main hospital notes.

Now, I don't know whether The London is different from other hospitals, but getting hold of the main hospital notes was often a nightmare, and when people turned up in the hospital for treatment, if they had a bleed, you needed to know who they were,

what their condition was and what they were treated with.

I think John Perrin's idea was to have this folder that would contain the main facts about the patient in the department and that meant that if somebody turned up in the middle of the night, or indeed during the day for that matter, the person on call could go to that folder and know they got the right information and treat the patient quickly.

I don't believe, and maybe we will come on to this, but I don't believe there was ever anything in those folders that were not in the hospital notes. Now the only difference between the brown envelope and the red envelope was that they were originally brown manilla envelopes and they tended to wear out and they were eventually replaced by red plastic ones.

Q. Just so that I can understand, because you know, I think, Dr Colvin, the issue of medical records, and what has happened to medical records is an important issue for the Inquiry, and we may come back to that, but in this period, 1977 through to the early 1980s, what would have been the various different types of notes and records that you would have had access to?

A. So obviously no computer. The notes are all handwritten, and there would be a system of

handwritten notes for each clinic secured by star clips. So you have a -- my service would be a big thick file with star clips, and I would write in the notes. For the rheumatology clinic there would be a separate set secured by a star clip.

For in-patient notes, each individual in-patient admission would be a paper copy separate from the next admission. The results were in a separate file, also secured by a star clip, and stuck onto sheets, which often the glue failed, and so they tended to be less than perfectly placed.

I'm afraid that -- there were secretaries in the ward, and indeed I had a secretary whose job was to try to control the avalanche of paper. I'm afraid I was pretty obsessional and spent a lot of my time trying to tidy up these dreadful notes. They, of course, were being moved around the hospital, so often you couldn't find them because a patient had been to a clinic somewhere and they weren't available or had been lost.

So I don't think The London was the worst hospital in the world for making the notes tidy and available but this difficulty used to trouble me a great deal.

Q. In relation to the red and brown envelope that you

described, where were those kept?

A. The red and brown envelope were kept in the department. So when I --

Q. In the Haematology Department?

A. Yes. I mean, the department also was barely a real department. What we had was, on the first floor of the main block there was a secretary's office, and it was in the same place as the laboratory. Professor Jenkins had his office and maybe we young physicians had a space where we could do things. I think there was also a small area reserved for patients who could be seen in what we might describe as "the department", if they weren't in the Emergency Department. The red and brown envelopes were kept with my secretary's area, and there would be access to them in the middle of the night presumably by getting a key and opening the department to get to the records.

Q. Then I understand that other notes may have been in other locations within the hospital depending upon where the patient might end up, but in terms of your own clinic notes -- so the handwritten notes you would make when you saw a patient and diagnosed them or proposed a course of treatment and so on, took blood for tests, whatever it was -- where would those notes

be kept?

A. That would depend on how severely affected the patients were, because I think we did keep the severely affected patients' notes in the department in a stack where we knew we could get hold of them. But for a mildly affected patient who perhaps either came once a year or didn't come up for years on end they would be in the main hospital records and we would call them up if we needed them.

Q. I want to move on, Dr Colvin, to consider your own and the developing knowledge of risks of viral transmission from blood and blood products.

Can I start by asking you what did you learn about those risks during your general medical training and your specialist haematology training?

A. So in '63 to '66, at university, that was just when the Australia antigen was described, so hepatitis B. I'm sure that in my general haematological training and in my training at the blood transfusion centre at Brentwood I would have been advised, and it would have been explained to me, all about hepatitis B transmission by blood and blood products. But of course by the time I came to certainly a consultant position, there was virtually no hepatitis B transmission going on anymore. But we were fully

aware of the fact that hepatitis B was a transmissible agent and was transmissible in blood products.

Q. Other than what you learnt during your training, what was your -- what were your means of keeping up to date with knowledge? First of all, what journals or magazines would you read?

A. So, I mean, very much like Mark Winter, I read the British Medical Journal, I read The Lancet and I read the New England Journal of Medicine as my weekly diet of information. In addition, I would read the British Journal of Haematology on a very regular basis. Of course I would see other journals as well but that was the core of my reading.

Q. What other sources of knowledge were there? If we start with UKHCDO, in terms of the reports that might be generated for example by Dr Craske and the Hepatitis Working Party for either for Reference Centre Directors or for annual general meetings, if a report was simply going to the Reference Centre Directors, you presumably wouldn't see that?

A. No, I wouldn't.

Q. Were the minutes of Reference Centre Directors meetings disseminated more widely to other directors?

A. I don't know but I doubt it. I really don't know.

Q. Then in terms of the annual meetings to which all

directors were invited, were the minutes of that circulated to the directors afterwards?

A. I would think so, and I was a regular attender. There would be very few annual meetings of the UKHCDO that I didn't attend. I'd be surprised if I didn't attend any.

Q. As far as I can tell from the minutes, there were reports produced, for example, by Dr Craske or by other working parties. It looks as though they were circulated in advance of the meetings for directors to look at?

A. Yes, I mean, I think that the UKHCDO had a good record of information dissemination.

Rosemary Spooner, who deserves a mention in any forum of the discussion of haemophilia care, was the data handler at Oxford, and was the most remarkable -- a remarkable woman, who really was able to mastermind the data collection and the work of the UKHCDO and the dissemination of information about UKHCDO's work, and it was a very important work that she did.

Q. So there's UKHCDO. You obviously had this close working relationship with, in particular, Dr Kernoff of the Royal Free Hospital?

A. Yes.

Q. Were there any other particular sources of knowledge

or information available to you -- I'm talking here really from 1977 through to the mid-1980s?

A. I don't think so.

Q. I'm going to look at an extract from your evidence to the Archer Inquiry.

Henry, it's ARCH0000012, please. Henry, if you look towards at the bottom of the page, I don't know whether you've got the whole transcript. We need to go to page 140 for Dr Colvin's evidence. If we just go back to 138.

We can see there, halfway down the page, Dr Colvin, this is the start of your evidence.

A. Yes.

Q. Then if we go over, please, Henry, to page 140 and picking it up halfway down the page, you said this:

"The statement I really wanted to make was that I am aware of the fact that liver infection became a feature of blood transfusion in the 1940s, that from the 1970s, the beginning of the 1970s ... it was quite clear that the concentrates were capable of transmitting hepatitis and that by 1975, the haemophilia treating community was aware that there was at least a possibility of chronic liver disease in haemophilia."

That is correct, is it?

A. Sure.

Q. Then what do you recall learning, and roughly when, about non-A, non-B hepatitis? You have referred to hepatitis B.

A. Well, I think that the term "non-A, non-B" gradually became adopted during the 80s particularly but very late 70s to 80s you would be able, perhaps, to inform me. But it doesn't make much difference really in the sense that we knew that there were abnormal liver function tests in people with haemophilia who had been treated by concentrates. In fact, of course, some people developed overt hepatitis. I mean, two or three of my patients, probably maybe up to half a dozen, had a significant attack of jaundice and hepatitis, which of course made them really quite unwell. They all always got over that. Obviously it's possible to die of acute hepatitis, even I think of non-A, non-B, but nobody -- very few did, not under my care.

So we did have quite clear evidence of jaundice and liver infection in some patients, but it was also known that people who hadn't had acute clinical hepatitis had liver function tests that were not necessarily normal. Some of them were normal, but most of them weren't normal. That's what we were

thinking about in -- perhaps particularly in the mid- to late 1970s and then into the 1980s as to what does this actually mean?

Q. So you were aware from probably the mid-1970s that there was this further form of hepatitis?

A. Yes.

Q. In fact, I think the literature does start calling it non-A, non-B hepatitis in the mid-'70s?

A. Yes, sure.

Q. The issue appears to be, looking at your statement, the question of how serious or severe it was understood to be?

A. I agree.

Q. We're going to look at some documents in a moment, but, first of all, what's your recollection -- picking matters up really when you've become a director and consultant in 1977, what's your recollection of your understanding of this condition?

A. Well, I think you need to put this in the context of the dramatic improvement in haemophilia care. I think we heard from many witnesses, either on television or in the last few days, how dramatic it was that haemophilia care improved, and people could do things they hadn't done before.

I think that physicians also were delighted that

they were able to offer people proper haemophilia care that changed their lives and I think people were reluctant to contemplate the possibility that there was "anything wrong" (in inverted commas) with these treatments.

So when we had patients who'd got chemical changes in their liver function tests that didn't make them unwell, and when we had people who were very well in themselves, I think there was the hope that this wouldn't be a big problem, and that hope clearly was misplaced.

However, the truth also is that it takes a very long time for most patients to get ill with hepatitis C or non-A, non-B alone, assuming they haven't had an acute attack. So Eric Preston wrote a paper -- I can't remember exactly when -- when he was able to tell us how long it took to get ill with serious liver disease, with non-A, non-B. It was -- something like 20 years was about the -- almost -- not the minimum, but, I mean, most people would not be ill for 20 years, in terms of things like cirrhosis or hepatoma. So I think that there was an unjustified but justifiable, if you like, feeling that it would be all right.

Q. I think the way you put it in your evidence to the

Lindsay Tribunal, it was more of a hope than based in evidence.

A. Absolutely.

Q. I am going to ask you just to look at a small number of medical articles from that time.

A. Yes, sure.

Q. They are materials that have been shown to you in advance. The first, please, Henry, is PRSE001431. I think I might have given you the wrong reference there. PRSE0001431.

That's it. So this is an article in The Lancet -- sorry, can we just have the date, please, Henry at the top of the page? 3 August 1974. "Long incubation post-transfusion hepatitis without serological evidence of exposure to hepatitis B virus."

So August 1974 in The Lancet -- I appreciate this is before you are a consultant, but it's whilst you're a haematologist. Would you expect to have read it at the time?

A. I think so, yes.

Q. Then we can see it's by Prince and others, and if we just look at the summary, first of all:

"An agent other than hepatitis B virus seemed to be the cause of 36 -- 71 per cent -- of 51 cases of

post-transfusion hepatitis identified during prospective bi-weekly serological follow up of 204 cardiovascular surgery patients. The sera of the 36 cases showed no evidence of the antigen or antibody response expected to accompany infection by HB virus and to be detectable by the sensitive assays used. Incubation periods and clinical and epidemiological features were inconsistent with hepatitis A."

Then we see, if we go to the last sentence:

"The data suggests a large proportion of long incubation post-transfusion hepatitis is unrelated to hepatitis B and that control of post-transfusion hepatitis will require identification of the hepatitis viruses type C."

In fact, not properly named type C for another decade or so. So there's the identification of non-A, non-B hepatitis.

A. Sure.

Q. Then if we go to the last page of the report, please, Henry, the sixth page. If we zoom in on the top left-hand bit. Thank you. Just slightly further down:

"The fact that non-B hepatitis cases are less frequently associated with serious acute illness does not imply that such cases are of lesser importance.

Long-term complications of acute hepatitis B infection, such as chronic hepatitis, cirrhosis and hepatoma, have been reported to follow mild anicteric infections more frequently than severe icteric cases; consideration must thus be given to the possibility that non-B hepatitis may play a role in the aetiology of some forms of chronic liver disease."

So we can see there a distinction being drawn between hepatitis B and non-hepatitis B --

A. Sure.

Q. -- in terms of the acute phase, which I think touches upon what you have already said, that you didn't see the acute illness particularly frequently.

A. Sure.

Q. But would you accept this is identifying at least the possibility of longer term complications that may follow not just with hepatitis B but also with non-A, non-B hepatitis?

A. Yes, and of course, indeed, it also points out that there might be hepatitis C, D, E, F, G, H, I, J, K. That it wasn't necessarily one virus -- assume it was a virus which was very likely.

Q. Then if we look, please, at an article which you have referred to, Dr Colvin. It's PRSE0001794, please.

So we see on the right-hand side "Factor VIII

concentrate". This is authored by Craske, Dilling and Stern and you have referred to this?

A. Yes.

Q. Presumably something that you saw at the time?

A. It's a key paper. I mean, it's a famous paper.

Q. What can you tell us about your understanding of its significance?

A. Well, I think what it says on the tin, in a way. What it says is there's an outbreak of jaundice in patients who have had freeze dried concentrate, and it wasn't hepatitis B.

Q. This was the -- an analysis of an outbreak that had happened in Bournemouth:

"Seven cases of non-hepatitis B, four of hepatitis B occurred within six months of the first use of this product."

So was this particularly significant for haematologists such as yourself because this is talking about patients who've received Factor VIII concentrates?

A. Yes. I think it's an important paper, and -- obviously I don't remember the detail of it, but Craske, Dilling and Stern is a paper we talk about.

Q. Yes, and I think you described it in your evidence to the Lindsay Inquiry as something of a watershed

moment?

A. I think it was very important.

Q. We'll just look at perhaps what's said on the second page of the report please, Henry, in the discussion. It's bottom of the page, please, under the heading "discussion" thank you:

"The measures now used by the National Blood Transfusion Service to reduce the incidence of transfusion hepatitis, such as the use of single donations and small pools of plasma, make the occurrence of more than one case of transfusion hepatitis as the result of contamination of a plasma pool by a single donor most unlikely. The risk is greatly increased with Factor VIII concentrates prepared from pools of more than a thousand donations. When blood for transfusion is prepared from commercial donations this increases the frequency of jaundice three to ninefold for single transfusions. The pool size however may be critical in Factor VIII concentrates, since transfusion hepatitis is a known hazard with large-pool products prepared from volunteer donors in the UK."

So am I right in understanding that one of the significant aspects of this paper is the attention it draws to the relative risks that may be associated

with different pool sizes?

A. I think it does and I think it actually underestimates the reality because, as we will see later, the reality was that if you've got a large pool concentrate with a national prevalence of hepatitis C infection of something like 0.3 per cent (I quote, although other people quote slightly different values), you've got thousands of donations at a prevalence of 0.3 per cent, hepatitis is inevitable. So I think this actually slightly underestimates what we now know to be the truth.

Q. The way you put it in your evidence to the Lindsay Inquiry -- we can look at it if need be -- but you talked about this as a moment, a watershed moment, after which it was known there was quite a significant problem for the future, at least in terms of numbers?

A. Yes, I think that's fair.

Q. So do I understand that to mean this was going to be a problem that might affect a significant number of patients?

A. Yes, I think that's fair. I think what wasn't known was what the problem was that would affect them. We didn't know what was going to happen next but I think we knew that it was going to happen to a lot of people.

Q. So that was August 1975. We know, obviously, within the Inquiry and those listening of the World in Action documentary "Blood Money" broadcast in December 1975. Do you recall whether you watched it at the time?

A. I don't recall that I watched it at the time. It's quite likely that I would have done. I've certainly seen it since.

Q. Do you recall whether there was any generation -- sorry, whether the programme generated any discussion amongst haemophilia directors at the time?

A. I don't recall that actually, but I'd be surprised if it didn't. But I really can't recall.

Q. Would you accept that by the mid-1970s hepatitis B was known to be a serious condition that could have severe long-term consequences?

A. Of course.

Q. What was the basis for assuming, if clinicians did assume, that this other virus (non-A, non-B hepatitis) would take a significantly different course?

A. Well, you might say it was wishful thinking but the fact that one virus has one set of characteristics doesn't mean that another virus will have the same set of characteristics. So whilst I think the point was made that there was no reason to believe that non-A, non-B (hepatitis C) would have a different course from

hepatitis B, there was no reason to believe that it would have the same course. I mean, it's a matter of experience.

Now, of course, what then happens is what are you going to do about the abnormal liver function tests? There's no test for the virus. There's no valid test for the health of the liver in that time, I think, that is anything other than a liver biopsy, and you may want to come on to the question of, "Well, do we do liver biopsies or don't we?"

MS RICHARDS: Well, I note the time, sir.

We will come on to that after the break, I think, Dr Colvin.

Sir, is that a convenient moment to break?

SIR BRIAN LANGSTAFF: Yes.

Can I just ask you this: during the war, it became apparent that after transfusion hepatitis might result. That fact was a given.

A. Sure.

SIR BRIAN LANGSTAFF: The general understanding was, as I read it, that that was known as serum hepatitis, to distinguish it from hepatitis A, as it later became known, which was infectious hepatitis.

A. Yes.

SIR BRIAN LANGSTAFF: The course of serum hepatitis might

involve an acute phase, it might involve a chronic phase and it was generally understood that the chronic phase could result in long-term cirrhosis, long-term serious liver problems, including cancer. All that was known before --

A. Yes.

SIR BRIAN LANGSTAFF: -- the constituent parts of serum hepatitis were discovered, first of all, hepatitis B and then later on non-A, non-B, which became largely known as hepatitis C. So by the time that you went into training, it would have been appreciated that hepatitis caused after transfusion could result in very long-term consequences.

A. Yes, of course.

SIR BRIAN LANGSTAFF: So to think that -- was there a reason for thinking that by identifying hepatitis B, the serious part of what had been serum hepatitis had become known? That, I think, would be wishful thinking, would it?

A. I think everybody used the expression "wishful thinking" and I think you've just used it and I would happily use it again. I think it's true.

SIR BRIAN LANGSTAFF: So there would have been not only no reason to think that hepatitis non-A, non-B was less serious in its long-term consequences than hepatitis B

had been or other forms of serum hepatitis, would there? It would be wishful thinking to think otherwise. You just said so, I think.

A. I think that many of the patients didn't have an acute phase.

SIR BRIAN LANGSTAFF: No.

A. Many of them had rather minimal abnormalities of liver function in terms of their transaminase levels. I don't think there was any evidence either for or against the long-term consequences. If you say to me, well, this form of hepatitis had long-term consequences, then surely this type of hepatitis, other form of hepatitis, would have long-term consequences, the answer is, well, maybe, maybe not but there's no evidence. There was no evidence either way until we get on to the points that may be asked after the break. But I --

SIR BRIAN LANGSTAFF: We will see where we go after the break nevertheless. Thank you very much.

MS RICHARDS: Sir, sorry, would you give Dr Colvin the customary advice about not discussing evidence. He knows already.

SIR BRIAN LANGSTAFF: Yes, I will.

We will take a break until 12 -- no, let's make it 11.50, because I think there are probably less

people here today than there were last week.

You're giving evidence. You must not discuss anything about your evidence, either what you have been asked or what you think you might be asked, with anyone, whoever it is, but you can discuss anything else you like.

A. Thank you very much.

(11.12 am)

(A short break)

(11.50 am)

MS RICHARDS: Dr Colvin, I'm going to ask you to look at three further articles with me. They may or may not be materials you saw at the time, and that's one of the questions I'll ask you.

Henry, could we please have PRSE0000381. We can see this is an article. It's in 1976 in the Yale Journal of Biology and Medicine. "Non-A, non-B hepatitis". Purcell, Alter -- one of the recipients of the Nobel Prize for medicine yesterday -- and Dienstag.

Is it likely that this is an article you would have read at the time?

A. Not at all.

Q. If we just look at it, we'll just go, I think, please, Henry, to page 4, please. Picking it up halfway down

the page with the passage beginning "Although type non-A, non-B":

"Although type non-A, non-B hepatitis is associated with less severe acute illness than type B disease, as judged by frequency of jaundice and magnitude of SGPT elevations, the long-term prognosis for the two diseases may be similar. Thus, elevation of transaminase values persisting for six or more months has been observed more frequently following non-A, non-B disease and following type B hepatitis. Others have reported similar results. Transaminase elevations had been documented for several years in some patients. Three such patients at the NIH underwent liver biopsy. Two had histopathalogic changes in the liver compatible with chronic active hepatitis, and the other was diagnosed as having chronic persistent hepatitis. Thus, chronic non-A, non-B hepatitis is not necessarily a benign infection and may be the cause of a significant proportion of chronic hepatitis not identifiable as type B disease."

So we can see there, Dr Colvin, in this publication the warning, if I can put it that way, or observation that chronic non-A, non-B may have similar long-term consequences may not be a -- to hepatitis B may not be a benign infection.

Now, I understand that you wouldn't have seen, didn't see this article at the time. How would information and learning such as this, which would potentially be important for haemophilia clinicians to know at a practical clinical level, how would that be disseminated?

How would you expect as part of the structure of medical learning for that kind of information to filter down?

A. Well, obviously, if there are key papers in a journal that can be picked up within the medical literature -- something like The Lancet or the British Medical Journal may pick up such a thing, but more likely The Lancet than the British Medical Journal.

But really, you know, the best articles and the best information always came from the New England Journal of Medicine. I think that anybody practising any kind of medicine is well advised to read the New England Journal because it always contains the material which tells you what's really happening and has an enormous reputation for authoritative view on the current medical practice and the way medicine is going.

So I think that, whilst UKHCDO might be expected to disseminate this kind of information, they probably

would over a period of time. I think that the best way to keep up is the New England Journal.

Q. So for a haemophilia clinician such as yourself, not a liver specialist, your expectation at the time might have been that these kind of developments would be being picked up, say, by the Hepatitis Working Party of UKHCDO?

A. Yes, I think so.

Q. That would be a means of disseminating it more widely?

A. Absolutely. Yes, of course. I agree.

Q. Then if we just look at a couple of further articles before we turn to one which I'm fairly confident you will have seen.

NHBT0000092_002, please, Henry. This is 1977. It's a publication, Vox Sang. Is that something that you would have seen?

A. I didn't see Vox Sanguinis, no. Not on a regular basis.

Q. We can see, again, it's Harvey Alter speaking or writing. This appears to be a text of something delivered as part of an international forum. "How frequent is post-transfusion hepatitis after the introduction of third generation donor screening for hepatitis B? What is its probable nature?"

If we just go to the second page, Henry, really

on a theme with what we've looked at so far. Last paragraph on that second page, please, Henry. Further down. No, that's not it. Could we go further down, please. Sorry, Henry, to the next page. Do you have a further page? There should be. Thank you.

So we look at the last paragraph:

"Although non-A, non-B hepatitis is, on the average, less acutely severe than type B hepatitis, it can cause severe acute disease, and more disturbing, it appears to have considerable propensity to progress to chronic hepatitis. The major thrust of post-transfusion hepatitis research must now be directed at developing detection methods for the non-A, non-B agents, or developing some reliable method of viral inactivation or removal which would be independent of testing."

So, again, there appears to have been a recognition here in 1977 of the potential for progression to chronic hepatitis.

Again, you would expect, as a haemophilia clinician, to glean that either from the more general medical journals or through UKHCDO?

A. Well, yes.

Q. The final of these three documents, Dr Colvin, is another 1977 publication.

Henry, it's RLIT0000228.

So this is a publication in 1977 in the Annals of Internal Medicine. Would that be something you would expect to read?

A. I'm afraid not.

Q. We can see it's authored by Hoofnagle and an array of others.

If we go, Henry, to page 6, please, right-hand column. There's a paragraph beginning:

"Several clinical and epidemiologic features of non-A, non-B hepatitis have become clear from studies such as the present one."

I just wanted to go through the four features and see the extent to which they reflected your understanding, Dr Colvin, in the late '70s:

"So, first, non-A, non-B hepatitis closely resembles type B hepatitis. The incubation period, the clinical symptoms and signs, and the potential for chronicity appear to be similar to type B hepatitis. Undoubtedly what was once referred to as serum hepatitis included both type B and non-A, non-B hepatitis."

Would you say that was generally understood in the late '70s by you and your colleagues?

A. I'm not sure I would quite take that point of view.

I think I would take the point of view that there were similarities between hepatitis B and this entity, but I wouldn't necessarily want to compare them in quite that way, perhaps at intellectual level that there was no evidence that this was hepatitis B and, therefore, one would expect it to have some different characteristics. I completely accept that some of the characteristics were the same, but I wouldn't necessarily assume that because there were similarities that they were going to behave in the same way. But I think one should be aware that it might do.

Q. Yes, and I think in fairness to this paper, it's based upon specific studies. I'm conscious they're not studies you read at the time. So I think the first point here may be more than an assumption by this stage but based upon studies.

The second point then is:

"Second, non-A, non-B hepatitis appears to be spread predominantly by the parenteral route."

Then most of the cases described an association with transfusion, intravenous drug use, or serum inoculation. That was, I think, was well understood?

A. I think that's a key point, really, that it's a parenteral spread; that is, it's not spread by

mouth. So in that sense, of course, it's very similar to serum hepatitis. That's the way it's spread.

Q. Then the third point is:

"Non-A, non-B hepatitis appears to be associated with a chronic carrier state and chronic liver disease. In this study, sera taken from HBsAg-negative donors 149 to 385 days after an implicated transfusion were found to be infectious. These implicated blood donors were, for the most part, asymptomatic, although liver function tests and liver biopsy examinations frequently showed evidence of underlying chronic hepatitis."

So, again, thinking of your state of knowledge of what you would have expected you and your colleagues to know in the late 1970s, is it fair to say that you would, by this time, have been aware that there may be an association between non-A, non-B hepatitis and chronic liver disease?

A. I think that's fair.

Q. Then the fourth point:

"Non-A, non-B hepatitis appears to be common."

That, I think, was also increasingly or commonly understood?

A. I think we didn't really know that until there were studies of hepatitis from particularly cardiothoracic

surgery from the blood transfusion risks in cardiothoracic surgery. Then it became apparent that the prevalence in the United Kingdom community might be as high as 8.3 per cent. So I think that, in those days, we didn't expect that hepatitis C would be so common and prevalent in the United Kingdom community.

Of course, worldwide, there are huge differences in the prevalence of hepatitis C. I think perhaps the most prevalent area is -- perhaps Egypt is one of the countries that's very prevalent. But I think we were a bit surprised that it was as prevalent as it is.

Q. So if I understand your answer correctly, again, looking at it in the late 1970s, you weren't necessarily aware of its prevalence amongst the wider population --

A. Yes.

Q. -- which would include the donor population --

A. Yes.

Q. -- but it was, I think, widely understood to be a common consequence of blood transfusion and use of blood products?

A. Exactly.

Q. Then if we can look next at the publication by Professor Preston in 1978 in The Lancet. It's PRSE0003622, please, Henry. We can see it's published

in The Lancet September 1978. "Percutaneous liver biopsy and chronic liver disease in haemophiliacs."

You would expect to have read this?

A. Certainly.

Q. Do you remember reading it?

A. Oh, yes.

Q. So we can see it's authored by a number of clinicians I think most, if not all, of whom were haemophilia clinicians?

A. Well, Dr Underwood is a histopathologist. He was Professor of Pathology and became president of the Royal College of Pathologists.

Q. Professor Preston who we'll be hearing from -- obviously, a haemophilia clinician; likewise Dr Mitchell who we'll be hearing from, and I think Dr or Professor Blackburn was also a haemophilia clinician.

A. He was certainly -- he was one of the early members of the reference committees or the Reference Committee.

Q. Then we can see, if we pick it up, first of all, in the summary:

"Systematic screening of 47 haemophiliacs in Sheffield revealed abnormal liver function tests in 36 -- 77 per cent -- with a tendency for these abnormalities to persist. To assess the

importance of these abnormalities, percutaneous liver biopsy was 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. The liver pathology bore no relation to clinical history or to biochemical findings. Hepatitis B virus markers were common, but evidence suggests that this is not the only factor contributing to the development of liver disease. The high incidence of chronic liver disease seems to be a recent development and is probably related to factor concentrate replacement therapy."

So I think there are a number of things one can draw from that summary.

A. Yes.

Q. First of all, this is work being undertaken by haemophilia clinicians based upon studies on haemophiliacs?

A. Yes.

Q. Including by biopsy, which as I think you already pointed out was one of the few if not only methods available to actually examine the liver at the time, and it showed a wide spectrum of disease in a high number of the patients examined, including cirrhosis.

Then what was your understanding or what would

have been your understanding of the sentence:

"The liver pathology bore no relation to clinical history or to biochemical findings."

A. I think I already indicated that really in my answers so far -- was that many of the patients had no symptoms, and that didn't mean that there wasn't development of liver disease. I think it's important to understand that in many medical conditions there's a reserve, if you like, of function, and you don't get ill with liver disease until your liver really is in a very poor state. Similarly, in haemophilia, if you have a level of 5 per cent Factor VIII, you can get on pretty well in your life, and only if you have a serious problem do you get abnormal bleeding. So there's a lot of reserve in biological systems, and this is a good example where you can be potentially unwell for many years without being actually unwell.

Of course, it is the case that we now know that many people with hepatitis C suffer from fatigue syndrome. I don't think that was an issue in the '70s. Nobody somehow perhaps noticed. But I think the main symptom of hepatitis C, or non-A, non-B, we now know is probably chronic fatigue.

Q. So would it be fair to say that this would suggest that clinicians could no longer work on an assumption

that the fact that a patient was not presenting with any overt or acute signs of hepatitis or appeared clinically well was not a reliable indicator that they weren't going to develop non-A, non-B hepatitis?

A. That's true. I would like, if I may, if I'm allowed to do so --

Q. Absolutely.

A. -- to introduce another paper from 1982. Now, this is a paper from Pierre Mannucci and Colombo and Rizzetto in Blood. I can give you the reference.

Q. I am not sure whether we have it available to screen, but if you --

A. The reference is Blood, 1982, volume 60, and it begins at page 655, and it's entitled "Non-progressive course of non A, non-B chronic hepatitis in multi-transfused haemophiliacs".

So, as I'm sure you're aware, Professor Mannucci is one of the most distinguished international figures in haemophilia care. What he and his colleagues did was look at eleven people with haemophilia and what they found -- I won't go into the detail because it's not appropriate, but what they found was that there was evidence of non-progression or even improvement in hepatitis condition, including on biopsy.

So I suppose for those who wanted to believe

that it wasn't a problem, then they could try to rely on Mannucci's paper from '82. But the reality is that the Sheffield group, whether we think it was sensible to biopsy people with haemophilia or not -- and that's another issue -- the Sheffield group has very long history of achievement in identifying these problems. Of course, you will be hearing from Professor Hay later who is, I think, now the greatest expert in the United Kingdom on this issue, and it was in Sheffield that he began to really focus down on this problem. He's not on this paper, but it's Charlie Hay's work in hepatitis, initially in Sheffield and later wherever he went to practise, that really shone the main light on this issue.

Q. If we just look at another document from 1978, Henry. It's CBLA0000831.

That's towards the end of it. Do you have an earlier page, Henry? Is that the only other page you have? You don't have the whole document?

We may come back to that. For present purposes, let me just tell you what it is rather than leave you and those listening hanging. It's a report from Dr Craske, and it's a report of the Haemophilia Centre Directors Hepatitis Working Party from 1978.

A. Yes.

Q. The bit I was going to show you, but I'll just read it out. It's in a discussion of chronic hepatitis, and Dr Craske reported a visit to the Department of Medicine at the University of North Carolina during a visit to the States, and he says:

"I had the opportunity to discuss the problem with Dr Roberts and his colleagues. They have carried out almost 100 liver biopsies on patients with chronically elevated serum transaminases in a collaborative survey, and nearly 50 per cent of these have histological changes compatible with cirrhosis, chronic active or chronic persistent hepatitis. These patients have had up to ten years of treatment with freeze-dried Factor VIII concentrates of different brands."

Now I'm sorry we don't have that to actually show to you, Dr Colvin, and we can potentially rectify that later but that's a report of a much wider number of biopsies made by Dr Craske which he presented to a directors' meeting at which you were present in November 1978.

Do you have any recollection of that information?

A. No, I don't.

Q. I appreciate I'm asking you about events over 40 years

ago. You would no doubt have read the report that was circulated in advance of the meeting?

A. No doubt.

Q. Do you think that's something that would at the time be likely to have struck you, that number of biopsies, with that level of --

A. Well, I think I was struck by Professor Preston's information. I mean, I think I was -- I would have been struck by this as well. I mean, I think we appreciated that there was potentially a problem. I only introduced Professor Mannucci's paper to just give an explanation of why perhaps it was that some people didn't want to believe it.

Q. Would you put yourself in that category in retrospect at the time of someone who didn't want to believe it?

A. I don't think I would, but I would also put myself in the group of people who didn't know what it meant and didn't know what to do about it, because there was nothing to be done at the time.

Q. We'll come on to that and what information could have been given to patients and so on in a few minutes.

There are a couple of further documents, which are ones which I hope we will be able to bring up on screen, which are ones that you would have seen at the time.

BART0002487, please.

This is a letter dated 27 April 1979. It's from Dr Kernoff to you. We may come back to the letter when we look at your treatment policies in more detail, but if we just go, please, to the second page of the letter -- sorry, yes, I think it's the second page. Yes.

Under the heading, "Types of therapeutic material available", if you could just zoom in on that paragraph, please, Henry. As I say, we may come back to some of this, but if we go about halfway down that paragraph it says:

"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 [et cetera]. We may, therefore, be introducing diseases which are not yet endemic in the UK."

So leaving aside that latter point, Dr Colvin, which I think you've already made, about not knowing

the prevalence in the wider population, we can see here Dr Kernoff writing to you describing non-A, non-B hepatitis in 1979 as a serious disease with long-term consequences. So it's fair to say that would have represented your knowledge by that time in any event?

A. Of course, yes.

Q. Then if we could go, please, Henry, to BART0000684, please.

So this is -- if we just go to the third page, first of all, Henry -- we can see this is a document co-authored by Dr Kernoff and you on 16 May 1979. Then if we go back to the first page:

"NETR Association of Haematologists: Haemophilia Working Party."

Just before we look at the body of it, we mentioned this earlier and I was going to come back to what the Association was. Could you just tell us what was the North East Thames Region Association of Haematologists and what in particular was its Haemophilia Working Party?

A. So we had a group of consultants in the North East Thames region of the various different hospitals, and we just got together and the Association of Haematology itself nominated a working party of interested physicians.

Q. We'll see later that you met at this time on a regular basis and discussed a range of issues?

A. We did, yes.

Q. Then this is:

"Guidelines on the screening and investigation of hepatic disease in patient with congenital coagulation disorders."

Under the heading "Background" you say this:

"During the last few years it's become increasingly recognised that a high proportion (eg 50-75 per cent) of patients with haemophilia and Christmas disease having active replacement therapy have sustained abnormalities of plasma liver function tests. To elucidate the causes of these abnormalities several groups of investigators have recently carried out liver biopsies in selected patients."

That's a reference in the footnote to a publication by Spero and others in the New England Journal of Medicine, and then also to Professor Preston's that we've just looked at:

"A wide spectrum of histological abnormalities has been found (chronic active hepatitis, chronic persistent hepatitis, fatty infiltration, micronodular cirrhosis) but the type and severity of the abnormality correlates poorly with the results of

liver function tests."

So is that the mismatch that you described?

A. I think it is, yes.

Q. "The primary cause of liver disease in haemophiliacs is unknown, but thought to be most probably related to multiple transfusions. Infectious agents such as various hepatitis viruses have been particularly incriminated, but there are other possibilities such as immune complex disease and the effects of denatured proteins."

Then if we go on to look at the second paragraph, please:

"Of possible particular relevance to chronic liver disease in haemophiliacs is transmission by factor concentrates of the agents responsible for non-A non-B hepatitis. This group of disorders has recently come under close scrutiny because of the realisation that the majority of cases of post-transfusion hepatitis in some parts of the world -- in particular, the USA -- are not due to hepatitis A or B viruses or any other recognised infective agent. At present, there are no specific laboratory tests available for non-A non-B hepatitis and it seems likely that many cases are sub-clinical, or at least non-jaundiced. Recognition of the disease

may therefore necessitate serial liver function tests being carried out after transfusion of possibly infectious material. For practical reasons, this could only be undertaken in patients at particularly high risk."

Just pausing there, what you seem to be saying there is that there may need to be serial, as in repeated, on an ongoing basis, liver function tests.

Why is it said there that for practical reasons that could only be undertaken in patients at particularly high risk?

A. Well, I think that's quite a difficult question to answer.

"Recognition of the disease may therefore necessitate serial liver function tests ..."

That makes sense. But liver function tests aren't difficult to perform. They are easy to perform and so, if it means that we should keep an eye on the liver function tests of people with haemophilia, then I don't think that that particularly relates to people at particularly high risk. So I find that quite difficult to understand.

Q. Okay. You share my confusion then, Dr Colvin. I was unclear as to who was this cohort of patients at particularly high risk.

Would that have been potentiality severe haemophiliacs?

A. I suspect it might have been.

Q. Is that the reference to "practical reasons" because they are the ones you are seeing on a regular basis and can follow up?

A. I think that is fair but the difficulty, of course, is that we now know that anybody who received the large pool concentrate, however often they received it, would have been infected with hepatitis C. So the other thing that might have been thought of in this context was maybe one should look at people carefully who had been treated with commercial concentrate rather than NHS concentrate. But the reality was, we now know, that whether it was commercial or NHS there was inevitable infection with HCV.

Q. This paper appears to recognise that broader risk. If we continue it says:

"Amongst haemophiliacs it seems likely that one risk factor is previously infrequent transfusions, since the patient will have been less likely to develop immunity to the disease. Another is probably a change in usual therapy from cryoprecipitate to concentrate, and perhaps a change from one type of concentrate to another. Whether commercial

concentrates pose a greater risk than NHS material is uncertain. It is known that both commercial and NHS factor VIII and factor IX concentrates may transmit the disease."

So it would appear by this time, middle of 1979, you and Dr Kernoff understand that non-A, non-B can be transmitted both by commercial and by NHS?

A. Indeed. But you can also see, I think, in these sentences a degree of confusion and, indeed, inaccuracy, as we now know. I mean, I'm sure when we wrote these words we meant them and we believed that they made sense, but now we look back we can say, well, some of this isn't actually quite right.

Q. And, as it were, for the record, can we just identify what the bits that you would now say are incorrect are. The concept of immunity?

A. Well, I'm going to go back a bit further. I mean, one of the things that is clear, I think, is that either commercial or NHS concentrate will inevitably transmit non-A, non-B hepatitis C. That although serial liver function tests have got some value, there's no correlation necessarily with the progression of liver disease. It may be that we thought that people who had been given commercial concentrate had particularly high risk. That wasn't true. Maybe we wondered

whether the subtype of hepatitis C, as it then became, transmitted in the United States was different from that in the United Kingdom. That may be true. Then we would have to ask ourselves whether that particular type of hepatitis C was more dangerous than the UK hepatitis C. That may or may not be true.

The idea was that if one had less frequent transfusion they would be less likely to develop immunity to the disease. Well, actually, I don't think it's got anything to do with immunity to the disease really. I mean, 10 per cent of people with hepatitis C do become immune and don't get into trouble with the liver. The other 90 per cent of course do and I don't think that's got anything to do with the frequency or infrequency of transfusion.

Maybe a change in usual therapy from cryoprecipitate to concentrates might be important. Yes, it is. Maybe a change from one type of concentrate to another might be important. No, it isn't and, no, commercial concentrates don't pose a greater risk than NHS material.

So I can now pick all sorts of holes in my words of years ago.

Q. Then if we go to the next paragraph, we can see you say this:

"Despite the generally mild nature of acute non-A non-B hepatitis it seems very possible that there may be serious long-term sequelae and the acute disease may sometimes be fatal. It is particularly for these reasons that closer monitoring of patients than has hitherto been the case as is now be, advocated."

A. Yes, very fair.

Q. If we now go back to the main paper, please, Henry, we see you go on to discuss the ethical problem of liver biopsy and record a difference of opinion within UKHCDO.

If we go to the second page, please, Henry.

As I understand it, Dr Colvin, the course adopted at The London Hospital was not to undertaken liver biopsies at this time?

A. There were very good reasons for that. Whether they were valid reasons, of course, is not for me to determine, but the Royal Free had done a liver biopsy in a patient, either before or after this, I'm not absolutely certain, but this patient had become ill and died, of bleeding.

Q. Yes.

A. The view at the Royal Free was that it was dangerous to perform a biopsy on the liver in a person with

haemophilia.

Now, this reflects an interesting aspect of medical practice in general, and that is if you get your fingers burnt once, you are very reluctant to have your fingers burnt again, even though, in the overall scheme of things, this procedure might be safe. Because of course the people at Sheffield thought it was safe and the people in Italy thought it was safe.

I was, as I explain, very much somebody who believed in the importance of teamwork and I believed, personally, and also in collaboration with the Royal Free, that these biopsies weren't a good idea. Now why might they not have been a good idea? Mainly because once you've got the biopsy material, it wasn't much use to you in making clinical decisions. Of course you could say to people, well, you should try to avoid excessive alcohol consumption, but you could say that anyway. There wasn't any evidence of any other particular benefit in knowing the answer since there was no treatment.

Now, you might also ask me, "Well, were you concerned, Dr Colvin, that it was expensive to do biopsy the liver?" Because you need a lot of concentrate to cover the procedure. Well, it would

always have been a thought that if one was giving a very large amount of concentrate for an investigation which put a patient at risk and cost a lot of money, it might not be a good idea. But of course other people take a different view.

Q. Then we can see that under the heading "Recommendations for routine management", you and Dr Kernoff set out an ongoing management process. You say:

"The general purposes of these recommendations are (a) to provide a database which will help us to understand and possibly contain a problem which at present is of unknown magnitude and (b) to more fully evaluate individual patients in order to aid better short and long-term management."

Then we can see the plan is, at A:

"All patients having replacement therapy at least once in any 6-month period should have plasma liver function tests [et cetera] checked at least once very 6 months."

Then B goes to set out where the liver function test is found to be elevated, that the test will be repeated on a monthly basis, and if this happens on more than two occasions the patient will be referred for further assessment.

You say there:

"The Directors of the Centres at the Royal Free and London Hospitals will be pleased to receive such referrals and will be working in collaboration with their local hepatologists."

At this point in time -- so in 1979 -- what access for these purposes did you have to hepatologists as opposed to the Royal Free?

A. Well, I would have had access to my own hepatologists, and I detail some of them in my submission, and indeed there are one or two others that I actually forgot. But I don't think that we had any real evidence of people who requiring referral at this time. This, of course, is reflected from Professor Preston's work where he showed that to get to the point where you needed to have a hepatological opinion could take many decades.

One of the things I think that this Inquiry was puzzled about was my evidence I think to Archer, or it may have been to Lindsay, that I saw very little hepatological disease in my patients who were not HIV positive. You sent me some information earlier, I think yesterday, showing that I'd actually reported that very clearly to Professor Preston.

So although I was willing to refer a patient to

a hepatologist in 1979, I don't think I referred anybody to them.

Q. Then we can see at C you say:

"Particular importance is placed on a sudden change in LFTs, a marked change in LFTs and suspicion of acute hepatitis. In all these instances early referral should be considered."

Does it follow from the answer that you have just given that you did not at this time or you do not recall seeing patients who had a sudden change in LFTs or a marked change or -- and suspicion of acute hepatitis?

A. I think it's important to appreciate that the LFTs tended to come and go in a quite sort of unpredictable way. So the normal LFT AST is, say, sort of 30, and many of these patients sort of had values of, I don't know, 60, 80, 120, and fluctuate as the visits went on. Now if a patient suddenly had a value of 2,000, that would ring alarm bells. So you can see the scale of the potential changes because if you have a level of, say 2,000, it implies a lot of inflammation of the liver very suddenly. No, I didn't see that.

Q. Then you talk at D about:

"Patients considered to be at high risk of developing non-A non-B hepatitis (see above) should,

where practicable, have blood samples for LFTs taken before and then at weekly intervals for 6 weeks after transfusion of the high risk material."

Does that help in understanding who you were identifying as the high-risk patients?

A. Well, I don't think it does very much. I think the main point is the attempts to identify people who were treated for the first time with a blood product as to whether they were getting into trouble. We now know, from 1985 anyway, onwards, that if you had a large pool concentrate you were bound to get hepatitis.

I think that we began to look, and we'll perhaps come on to this, at all our patients who were being given treatment for the first time to look to see whether they had a normal liver function test or not, because -- because the liver function test abnormalities were both intermittent and remittent -- by that I mean intermittent they were yes or no, remittent, coming and going, you could easily miss an episode of liver infection expression. So you could easily miss elevated LFTs if you didn't take samples very frequently.

You will see in later discussions with the studies on people who had not been previously treated, either untreated patients or infrequently treated

patients, that we often tried to follow these patients carefully before the days of the anti-HCV test to see whether there really was any evidence that they had had liver inflammation or not. That became key in looking at the concentrates that were regarded as being safe, or at least safer, from a non-A, non-B hepatitis C viewpoint.

Q. Leaving aside the issue of referral to the local hepatologist and leaving aside any question of liver biopsy, was this management programme that's set out here effectively the management programme that you implemented at this time at The London Hospital?

A. I believe so. I mean, I saw my patients regularly. I believe it is the case that patients very rarely came to the hospital without seeing me personally. Even if my junior staff saw them, I would still go and see them to say hello and to make sure that their visit had been worthwhile, and I believe that I did monitor their liver function tests with care.

Q. If we look at one further document from 1979, Henry, it's BART0000682, we can see this is an example of a set of minutes from the Haemophilia Working Party of the North East Thames Region Association of Haematologists. This is 12 December 1979, and you are there along with Dr Kernoff and others.

If we just go to the second page, please.

Under the heading "Regional Study of post-treatment Hepatitis", it says:

"Preliminary findings of the Regional Study of Hepatitis were discussed. Up to 70 per cent of severe Haemophiliacs have abnormal liver function tests at some time, with a wide spectrum of histological abnormalities.

"The Non A/Non B types of hepatitis appear to be most common.

"All types of Concentrate constitute a risk. There is, as yet, no evidence that imported Concentrates are more dangerous."

What, if anything, can you recall about the regional study of hepatitis?

A. I can recall nothing about this other than to say that I know, but I'm not sure of the dates, and you will have find out from Professor Lee, that she was recruited by Peter Kernoff to study hepatitis in this context.

Now when she was actually doing her work I can't recall, but she will tell you I think anything that was to do with research in the field of non-A, non-B in the North East Thames region, but of course also included North West region, but I don't know the

answer to that question. I'm surprised at this statement "with a wide spectrum of histological abnormalities", because I don't know where the histological abnormalities would be coming from, because I wasn't biopsying; I think neither was the Royal Free. So I think you need to ask Professor Lee that.

Q. Fine, I can do that.

Just still in March 1979, Dr Colvin, could we have BPLL0016050_003, please, Henry.

This is a report in The Lancet in March of 1979 from, amongst others, Professor Zuckerman, "Transmission of non-A non-B hepatitis to chimpanzees by Factor IX concentrates after fatal complications in patients with chronic liver disease."

You would, I assume, have seen this at the time as it's a Lancet publication?

A. I must have done.

Q. We can see from the summary what the subject of the article was:

"6 cases of non-A non-B hepatitis which followed administration of four different batches of concentrates of coagulation factor IX and commercial and non-commercial sources are described. Of 17 patients who received the concentrate on account of

chronic liver disease, 4 developed hepatitis, and in 3 of these the illness proved fatal. The incubation periods ranged from 42 to 103 days (mean 65 days). 3 chimpanzees were inoculated with concentrate from the same batch used on the above patients, a further commercial batch upon which no adverse reactions had been reported, and plasma from a known non-A non-B carrier. All developed hepatitis after 10 weeks' incubation."

Then if we go to the very end of the article please, Henry, so the last page.

If we look at the last paragraphs -- it's the left-hand side, please, Henry, left-hand column -- you can see in the last paragraph, the view of Professor Zuckerman and others:

"Until blood-donors can be screened for the non-A non-B hepatitis agent, it would seem wise to restrict the use of both commercial and non-commercial concentrates to life-threatening situations. In particular, their use in patients with chronic liver disease should be avoided, as the risk of a serious illness resulting appears to be increased."

Do you recall reading and considering that at the time, Dr Colvin?

A. I don't recall reading and considering it at the time

but I can certainly comment on it now if you would like me to do so.

Q. Yes, please.

A. So this paper is about people with chronic liver disease; it's not about people with haemophilia. The Factor IX concentrate was used to treat people who perhaps, when they are having a biopsy or something like that, I don't know exactly why it was used -- but we're not looking at people with haemophilia in this paper.

These physicians and pathologists are not haematologists. It's not a haemophilia paper. So I don't think we can necessarily extrapolate from this paper to haemophilia care, and I wouldn't support the last paragraph, in the sense that nobody in the haemophilia world, I don't think, thought that to limit commercial and non-commercial concentrates to life-threatening situations was remotely possible.

Q. We'll come on to that shortly because I want to ask you about your treatment policies.

Other than what you would have learnt from any discussions with Dr Kernoff and his colleagues at the Royal Free, and other than any analysis that may have been performed by the Hepatitis Working Party of the UKHCDO, are you aware of there having been at around

this time, late 70s/early 80s, any form of systematic assessment by haemophilia clinicians of the risks and severity of non-A, non-B hepatitis?

A. Well, as far as the risk was concerned, it was being looked at by the Hepatitis Working Party, and eventually there were the publications from UKHCDO which showed the incidence and prevalence of hepatitis C.

So -- eventually, of course, there was Peter Kernoff's famous paper in 1985, when it became clear that all patients were infected. But there was another paper earlier than that, from Oxford, which showed very much the same thing. So there was activity going on to demonstrate the truth but it required, I guess, by then, quite a lot of co-ordination. We weren't doing any academic work ourselves at that time in the late -- which year are we in here?

Q. This is 1979.

A. So we weren't doing any academic work ourselves in 1979 on this at The London.

Q. So you would, as I think you have already indicated in your answers, have been reliant in particular upon what UKHCDO and those involved in the Hepatitis Working Party were or were not doing?

A. Yes.
Q. And the advice that they were giving?
A. Yes. The Fletcher paper, I think which is particularly important, which is part of your compendium.
Q. Yes. I think you refer to that in your statement.
A. Probably, yes.
Q. Bearing in mind that by 1979 it was -- and I'm going to use your own words with Dr Kernoff's rather than any article you didn't read at the time -- it was recognised that non-A, non-B hepatitis could have serious long-term sequelae. Do you agree that that is information that should have been shared with patients at the time?
A. Yes, and I think -- we did share with our patients the reality that they had normal liver function tests and that that could be important for the future, but I guess, in retrospect, we should have been, no doubt, more -- clearer about what we feared. But I think that in communicating with patients one perhaps doesn't always communicate one's greatest fears. This is a matter of communication and the importance of trying to get communication right, but I acknowledge that there may have been many occasions when we didn't get the communication as right as we should have done.

Q. Without commenting on any individual patient, or indeed any particular patients that may have been patients of yours, a theme which has emerged from evidence received by the Inquiry on the whole has been patients saying that they were not aware at this time, late 70s/early 80s, of the risk of non-A, non-B hepatitis, and certainly there doesn't appear to be any guidance from UKHCDO saying, "Tell your patients".

Doing the best you can, do you think you would have had any discussion about non-A, non-B hepatitis with your patients around this time?
A. I probably wouldn't have necessarily called it non-A, non-B. I might have done. But I think I did monitor the liver function tests and we did discuss whether the liver function tests were normal or abnormal.
Q. But bearing in mind you have already said that may not actually be the best indicator --
A. No, of course not. I understand that.
Q. Do you think you discussed with your patients the fact that the treatment they were receiving or may have been about to start receiving carried with it a risk of a hepatitis virus that wasn't hepatitis B and that that might cause long-term chronic liver problems?
A. I think we could have done better.

Q. But does that mean you don't think you spelt that out to patients?
A. I mean, it's 40 years ago.
Q. I know.
A. But I think it's possible that the patients didn't get the advice or the information that maybe they should have had. But I can't say more than that, really.
Q. I may come back to that when we look at HIV again, the question of provision of information to patients.

I want to turn to look at the policies in The London Hospital under your directorship in terms of the use of different products.

First of all, I think your statement makes quite clear that once you became consultant in 1977 the decision as to what treatments to provide was a decision for you. There weren't others within the hospital who imposed any particular constraints upon you; is that correct?
A. Yes, of course.
Q. What role, as a matter of generality, again at this time, late 70s/early 80s, did the patients have in the choice of treatment?
A. I think that we didn't give them that much choice because we or I had a clear view about what was the correct treatment. I can go into a lot more detail if

you want about why I chose particular treatments.
Q. We will come on to that in just few minutes.

So if we take it in stages, if we just deal with prophylaxis, first of all, because I think that there's probably very little to say about that, your statement says that prophylaxis wasn't fully implemented until the 1990s. Was there any prophylactic treatment at all in the late 70s, early 80s?
A. Not really. I think Mark Winter referred to this in his statement, perhaps in his interview.

It was the case that if you had a patient with what is called a target joint, you might have a few days or weeks of attempted prophylaxis to sort of settle down a joint, but there really wasn't a concentrate for proper prophylaxis. I mean, Inga Marie Nilsson had thought of this years and years ago in Sweden, and I suppose we knew that it was a good idea to offer prophylaxis but there wasn't enough concentrate.

Even when we get, of course, to 1988, when we're using heat-treated concentrates routinely, that's reduced the yield of the plasma source that is being employed. So there's a tremendous world shortage of Factor VIII in 1988, and I've referred to this I think

in my paper, so that we didn't really start proper prophylaxis until the 1990s.

What happened was even then we weren't using really good prophylaxis. What I think Inga Marie Nilsson was trying to propose was that the level of Factor VIII should always be kept above 1 per cent, which is not very high, but actually we didn't achieve that. The result was a generation of young people with haemophilia who had been brought up in the 90s who had one or two target joints, pretty fit young people, but had one or two targets joints because they had been given prophylaxis that wouldn't really meet today's standards.

Q. So let's come on then to home treatment which was a feature of The London Hospital's haemophilia centre policies at the time. We've seen the figures: a relatively small number in 1977, increasing over the following years. Can I ask, first of all, what were the categories of patients to whom home treatment was offered?

A. Really people who were severely affected. There were one or two families where there was relatively mild or relatively severe haemophilia, with Factor VIII levels around sort of 1 or 2 per cent, who had significant repeated bleeding, and who were eventually selected or

invited to perform treatment.

The other big problem with deciding who was suitable for home treatment was also social circumstances. Now, as I'm sure you are aware, Whitechapel is one of the most deprived areas in the United Kingdom, with a huge immigrant community, many of whom speak no English, and so there was a challenge for me in deciding who was and wasn't suitable for home treatment within the severely affected group. Because if you're going to be on home treatment, you had to have a surface in your home, probably in the kitchen I suppose, where you could draw up and make the concentrates or the solution, and you had to record what you were doing, i.e. the actual treatment you were giving, and you had to be reasonably competent to give an intravenous injection and to understand when you would need to come to the hospital.

Now, if you didn't have any of those characteristics, you might think, well, surely we had a surface. Well, I can tell you that they didn't, and they didn't always keep proper records and they didn't necessarily know how to give an injection. Then it was very difficult to deliver home therapy. But I was also very surprised to find that some of my patients

I wouldn't have expected to have been good at home therapy turned out to be quite brilliant.

So it was really difficult to decide what families or which patients were actually the ones to give home therapy to when sometimes you had people who looked as though they were fine but were useless -- perhaps that's not the right word to use -- sometimes you had people who you thought to be fine but actually weren't and sometimes you had people you thought wouldn't be able to cope but did. So it was quite a challenge.

Q. So mostly those who were severe. Adults only or children as well?

A. No, children -- children, if one possibly could.

I mean, in fact, interestingly enough, this was where the domiciliary sister was so valuable. Because the domiciliary sister could go into the home and educate the families, and the children could surprise one very, very much. So you finish up with children, 3 or 4 or 5, taking an active part in their own home therapy and the delivery of the concentrate, even performing venepunctures within the home. So that really the work of the domiciliary sister and the attempt to get people onto home therapy was very important.

Of course we've heard previously from other witnesses the dramatic effect of being on home therapy. Suddenly you could go to school. Suddenly you could go to work.

I mean, I had three children, I think, who, as I became director, were at the Lord Mayor Treloar College, the college where there was the haemophilia centre for physically disabled children, and sadly all my patients who were there have died.

But whilst that was an extraordinary service provided by the Lord Mayor Treloar, I know it had weaknesses that you may have wanted to identify, it was wonderful to have children who could live at home, in a way which had become almost impossible with severe haemophilia.

Mark Winter made it very clear what a terrible disease haemophilia can be, and the provision of home therapy, of any kind, transformed people's lives.

It's also important to appreciate you don't need to do very much to make a big difference. So if you look at the Indian experience, Bangalore, Srivastava reported not so very long ago that introducing a system of care, albeit with very low doses of Factor VIII, in India, could transform lives using doses that we would think were grossly inadequate.

So there is a sense with haemophilia care, you get a lot for your first few units. You don't get much better from your last few units.

Q. In relation to home treatment, you began or the programme had begun using cryoprecipitate?

A. Yes.

Q. I will come on later to the pros and cons of cryoprecipitate, if I may, but then you moved on from cryoprecipitate to Factor VIII concentrates.

A. Yes.

Q. As I understand your statement, your policy for home treatment was to use NHS Factor VIII where possible?

A. If I could, yes.

Q. But sometimes it was not possible?

A. Yes.

Q. For supply reasons that we'll look at later.

A. Yes.

Q. And in those circumstances the family would have commercial concentrates?

A. Obviously, I can't recall the detail but I think it's almost inconceivable that I could have delivered NHS concentrate to all my patients on the home treatment for the whole of my career.

It's also important to appreciate -- and maybe this is the right time to mention it -- that patients

used to come in and out of my care, so that -- for instance, let's take the Treloar boys. They were partly in my care and partly not in my care. I couldn't control what happened to them when they were at the Lord Mayor Treloar College. I also had children who came under my care who had been at another centre whose treatment might or might not have been the same.

Of course now, in 2020, I can't recall exactly who got what in a way that I can reliably give you on both.

Q. In terms of home treatment, were patients required to keep their own records of the home treatment including batch numbers?

A. Yes, they were. It was a requirement.

Now, of course, this is very difficult because my view was that if you were going to have this very important and, for that matter, expensive treatment, you had to abide by the rules of the process. On the other hand, I've also pointed out to you, which I'm sure you will understand, that many of my patients were from very deprived communities and might have great difficulty in recording everything. They might not even be literate.

So there's a challenge in saying, "You can only

have this treatment if you do A, B and C, and if you don't do A, B and C, you can't have the treatment. Of course you can always come to the hospital to have the treatment in the hospital, but it's not as good as the home treatment."

So is there a sanction open to me, ethically if you like, to withdraw home treatment if you won't follow the rules?

I will leave that question open.

Q. Did the hospital also keep records of what particular batches were being given to particular patients for their home treatment therapy?

A. What happened was, we would record the home treatment therapy that was sent out, and then the patients would send back the information of what they'd used. But, of course, the two weren't synchronous. So it was actually very difficult in those days -- maybe it's even difficult today -- to do a proper sort of stock control of the treatment because it goes out and is kept in the fridge for a month, and then you get the results back one or two or three months later. Particularly if you had a patient who wasn't on a prophylactic regime, as they weren't to begin with, depending on how often they bled as to how often they -- they were meant to send the results in every month

but, you know, stock control got dissociated.

Q. So patients were expected on a monthly basis to, what, post the results to the hospital?

A. Yes, and we used to chase them.

Q. Did the development of the home treatment programme at The London have an impact on the adequacy of supply of NHS concentrate? Was more concentrate being used on home treatment than it would have been if patients were receiving their treatment in hospital?

A. Yes. I think that the truth is that the amount of concentrate used in home treatment was probably -- I think it was probably going to be a bit more than would have been used in the hospital because patients had complete control over how much they gave, even though they were given advice as to what dose they should give. They could give it immediately, and they could give it repeatedly if they wanted to. And certainly, not my job and not my -- I couldn't say you could only have one dose rather than three. If they were in hospital, I would say how much they were going to be given, and I would repeat it if I thought it was necessary. But, obviously, in a home treatment programme, you give people a lot of latitude, and that would tend to, I think, increase the dose and frequency, and of course, it would also increase their

health.

I would also say if you are going out to play, maybe -- and you've got a dodgy joint, maybe you should have a dose before you go. So there was this sort of rather limited sort of idea of sort of occasional prophylaxis, not a full prophylactic programme. But we tried to be sympathetic to the patient's needs in home treatment.

Q. Then in terms of hospital administration of treatment, so patients who were not on home treatment who were getting their treatment through their visits to the centre, is this right that they would receive, if they were severe haemophiliacs or receiving concentrates, predominantly commercial concentrates?

A. I don't think necessarily -- I think that the -- first of all, the very small children I tried to keep on cryoprecipitate right up to 1985. Now, it's very important that the Inquiry doesn't think that I saved the lives of all my children. I absolutely did not. The idea was that if a child came into a hospital and was an in-patient, then they would be given cryoprecipitate -- particularly very small children. The reason for that was that you don't need much Factor VIII to treat a simple bleed in a child. But if you have a child who's got a serious bleed or has

got a really bad knee joint, then it all becomes unrealistic, and so a patient would then be treated with a concentrate and, particularly if they were at home, they would be treated with concentrate.

So the number of my children, small children, who actually escaped any infection was actually I think quite small, but there were one or two. As far as whether they would receive commercial concentrate, I think we tried to give NHS concentrate if we could, and then for what I've described as disasters or emergencies or perhaps inhibitor patients or serious surgery, then that's when, probably, one would have to use commercial concentrates. But it's very difficult to have a precise rule about who gets what on a particular day and, of course, it eventually became very important.

But it's important for you to understand that I was an enthusiast for the NHS. Now, not all my colleagues were, and we tried to use NHS concentrates whenever we could, and we all regarded the commercial concentrates, which we did use, as a top-up for what wasn't available, and I believed in the NHS.

Q. We'll come and look at some availability issues when we look at some more of the North East Thames region minutes.

Just dealing again with, in general, the products that were used during this time. My questions are focused I think largely on patients with severe haemophilia.

A. Yes.

Q. In relation to patients with haemophilia A who were mild haemophiliacs, what was the main or first-line treatment for them?

A. Well, after '77 when Professor Mannucci produced his paper on DDAVP, then for really simple things, then one could rely on DDAVP and tranexamic acid and I used it. I think you can see that from the returns that you sent me a day or two ago, that I was using DDAVP and tranexamics on a regular basis. But DDAVP has many, many disadvantages which we can go into, perhaps, and should do. It's not a satisfactory treatment really for bleeding or for any important kind of surgery and so, in those circumstances, I think then we would probably be using concentrates.

Q. So for a mild haemophiliac who was having any kind of surgery other than dental surgery?

A. Well, of course, even dental surgery is not that easy because if you are having, say, a canine tooth removed, it's right at the front of your mouth, and if you use DDAVP and tranexamic acid for a patient with

a level of, say, 5 or 10 per cent, then you will get about threefold increase. From, say, 10 per cent you get to 30 per cent. You're using tranexamic acid. You might have just about two or three maximum doses of DDAVP available to you because of what's called tachyphylaxis, the level of response going off as you go on giving 12-hourly DDAVP because you're using up the limited resources of the body by using DDAVP. DDAVP releases what you've got into the circulation, and if you haven't got very much, you don't get much out. Once you've released it, it doesn't reproduce itself rapidly, and so you quickly run out of road with DDAVP.

So if you are doing a simple dental extraction -- I don't include, by the way, wisdom teeth extraction in this -- if you have a simple dental extraction, you can give DDAVP and tranexamic acid, give two or three doses at 12-hourly intervals, and then if the patient bleeds, you have a resource -- recourse, I should say -- to using a concentrate. But if you are dealing with an operation of any significance, or if you are dealing with a concealed problem like a bleed into a muscle, then if it gets worse when you're giving DDAVP, you've actually lost a lot of ground.

So I was never enthusiastic about using DDAVP either for any kind of concealed bleed or for any kind of serious surgery because I knew, from bitter experience I may say, that if you operate on somebody, or you give treatment for a muscle bleed, say, or a joint bleed and you -- it doesn't work, you go down a large snake, if you will forgive the expression -- in terms of snakes and ladders -- you go down a large snake and finish up with a patient with a really awful haematoma or a really serious bleed which then gets infected, and you've lost all that ground you could have gained by giving concentrate in the first place.

So, yes, DDAVP is wonderful. It's very useful for very mild haemophilia and mild von Willebrand's disease if you are not dealing with serious surgery or a concealed bleed, or if you've got a small open bleed that you can look at and deal with quickly, you know you won't lose ground, it's got a lot of value.

Q. We may come back to DDAVP and an article in relation to that after lunch. But just sticking with an overview of the products you used, moderate haemophiliacs, what was typically the way in which they would be treated? Was there a typical way in which they were treated?

A. Again, it depends a bit on the circumstances, but if

we're talking moderate haemophilia, we're talking about one or two per cent Factor VIII which means response to DDAVP is very inadequate, and I wouldn't use it.

Then you've got a choice of either cryoprecipitate or concentrate, and I think that we would choose concentrate for patients who have got significant bleeding or significant surgery who have got moderate haemophilia. That really is the treatment of choice. You may want to come on later to what I tried to do in '84 with a few patients with cryoprecipitate, and I'm happy to discuss that at some point.

Q. Well, I will come on to that --

A. But the answer to your question, I think, is that if you've got moderate haemophilia and you need treatment, then you need concentrate.

Q. Then von Willebrand's disease would ordinarily be treated with DDAVP?

A. Well, that's complicated as well because there are various different types of von Willebrand's disease. The majority are type 1, and they can be treated with DDAVP and tranexamic acid -- except perhaps for major surgery -- and even minor surgery or moderate surgery may require factor treatment. But type 2 von

Willebrand's disease -- I won't bore you with the detail -- is not necessarily ideally treated in that way with DDAVP. There's this thing called type 3 von Willebrand's disease which mostly is due to consanguinity in patients where their parents look normal but have a genetic defect which is multiplied by their consanguinity. Then you get very severe bleeding tendency which is completely unsuitable for DDAVP because it doesn't work.

Being in the East End, we had a large consanguineous problem because of the immigrant community, so I looked after I think a disproportionate number of patients with type 3 von Willebrand's disease who were not suitable for anything other than replacement therapy.

Q. Then patients with haemophilia A with inhibitors, what would the normal treatment have been for them?

A. So there is no normal treatment for people with inhibitors to Factor VIII. They very rarely get Factor IX inhibitors. I had one patient with a Factor IX inhibitor who very sadly had a cerebral haemorrhage and died early on in my career, so I can't really say much, if anything, about treatment of haemophilia B inhibitors.

But, as you will be aware, about 20 per cent of

people with severe haemophilia who, treated with Factor VIII concentrate, develop an inhibitor. Sometimes that inhibitor is weak, and sometimes it's very strong, and you can't be sure whether it's going to get very strong or not. If it's very weak, you may be able to use Factor VIII to treat it. It probably won't work. If it's fairly weak -- in the '80s, we used to give porcine Factor VIII, and the reason that worked was that the antibodies to human Factor VIII is less potent -- I'm sorry, the antibody to human Factor VIII is more potent against human Factor VIII than it is against porcine Factor VIII because the porcine factor has a slightly different configuration. So what tended to happen was that the antibody to human Factor VIII was perhaps ten times less active against porcine Factor VIII. So if you had a low-ish level of antibody to porcine -- if you had a low-ish level of antibody to human Factor VIII, then the porcine Factor VIII might actually work rather well.

Q. That would have been the Speywood porcine --

A. That would be the Speywood. That had a lot of advantages. Unfortunately, it also tended to cause very bad allergic reactions and also cause low platelet counts. We used it, and it had a lot of value before it was eventually withdrawn.

Q. What else would be used for patients with inhibitors?
A. The next thing you could use, if your human Factor VIII didn't work and your porcine Factor VIII didn't work (and you could probably predict from the potency of the antibody against human Factor VIII whether the porcine would work or not), then your next option was, in those days, FEIBA; that's Factor VIII Inhibitor Bypassing Activity. That was an activated Factor IX product produced in the United States.

So what was done -- oh, I don't know the exact technique, and it's probably a secret for all I know, and I think it was a secret -- they would take a Factor IX concentrate, and they would modify it in activating it in some way. What you were trying to do was to bypass the need for Factor VIII in the clotting mechanism, and it kind of worked.

Sometimes people used ordinary Factor IX for this purpose. So the ordinary Factor IX produced in -- either by, usually by BPL -- would have been activated a bit during its processing, and so it probably had some activated factor with it.

For instance, the ordinary Factor IX caused a lot of thromboembolism -- that is thrombosis -- in patients having orthopaedic surgery. If you had a patient with Christmas disease and you gave them

Factor IX, ordinary British Factor IX, many of them, particularly with orthopaedic surgery, would develop a thrombosis (either a thrombose arm or a pulmonary embolism) and it could be life-threatening. But these Factor IX concentrates, the less pure ones that we used to use in this time, had the potential for causing difficulty with thrombosis, but that could be used to benefit for patients with haemophilia A with an inhibitor, but the FEIBA was more activated than the ordinary British Factor IX.

Q. When did the FEIBA become introduced?
A. In the early '70s. And, of course, it would have also had just the same risk of transmission of disease.
Q. Then last category for present purposes, haemophilia B. Were they invariably treated with NHS Factor IX concentrates?
A. Can I just complete the discussion on inhibitors?
Q. Yes, of course.
A. Because in the '80s, recombinant VIIa became available for the treatment of inhibitors, but it was extremely expensive. And the difficulty was that neither FEIBA nor recombinant VIIa which was, of course, not a blood product as such -- neither FEIBA nor recombinant VIIa could reliably stop the bleeding. So Haemophilia Centre Directors were in a terrible bind really as to

what to do about people with inhibitors. If the human concentrate didn't work and if the porcine concentrate didn't work, then you were stuck with either FEIBA or later recombinant VIIa.

And it was always firefighting. It was extremely difficult and dangerous to initiate therapy -- for instance, surgery -- in somebody with an inhibitor and, of all the things I experienced in my whole career, the thing that kept me awake most at night was what to do about people with an inhibitor.

Q. Then Factor IX for patients with haemophilia B?
A. We used NHS Factor IX and, as I've explained to you, that NHS Factor IX was an intermediate purity product -- it wasn't a particularly pure product to begin with -- and it was very successful in managing Christmas disease, except insofar as the tendency to produce thrombosis in people having surgery, particularly orthopaedic surgery.

Of course, we were self-sufficient. Because Christmas disease is a sixth as common as haemophilia A, and because the half-life of Factor IX within the circulation is twice or three times the duration (so it lasted in the body longer), we were perfectly self-sufficient in Factor IX from the beginning.

MS RICHARDS: Sir, I note the time, and I'm going to move on to look at some documents that deal with issues of supply and shortfall in supply in the local area, so perhaps we could do that after lunch.
SIR BRIAN LANGSTAFF: Yes. Well, let's take a break then until 2.05.
(1.11 pm)
(Luncheon Adjournment)
(2.04 pm)
MS RICHARDS: Dr Colvin, I want to look with you at some minutes of the North East Thames Region Association Haemophilia Working Party from the late '70s/early '80s to look at some of the discussions that were ongoing about supplies of products.

Henry, could we have BART0000687, please. So we pick this up in February of 1978. We can see it's the Association of Haematologists (NETR), North East Thames Region Working Party in Haemophilia, and you're listed as present, along with the late Dr Dormandy, Professor Hardisty, Dr Tuddenham and others.

Can I just ask, who was Dr Carmichael?
A. Donald Carmichael was a consultant haematologist I think at Harlow but I'm not quite sure, and he was a sort of well-known figure in haematology in the region.

Q. Thank you. Then if we look down the bottom of the page, we can see under the heading "Supply of Factor VIII concentrate", Dr WJ Jenkins -- now, that's not Professor Jenkins?

A. No. John Jenkins was the director of the Blood Transfusion Centre at Brentwood.

Q. At this time, and then I think Dr Jean Harrison took over later?

A. Yes, she did.

Q. So:

"Dr WJ Jenkins said that Dr R Lane (now Director Designate of BPL) could increase his output by 25 to 30 per cent with additional equipment and staff but no extension to premises. He and Dr Dormandy had written to the Department of Health supporting this proposal and asked for the support of the working party, which was unanimously given."

So just pausing there. It would appear from this that there was a desire, supported by the working party, for BPL to be able to provide more Factor VIII for the region?

A. Absolutely because the Factor VIII concentrate, which may not have been the highest quality technically, that came from British donors was regarded, by me anyway, as the product of choice, and I wanted as much

of the NHS product as I could get hold of.

Q. If we look over the page, we can see Dr Dormandy reporting that the region would need 590,779 units of Factor VIII per annum to replace commercial concentrate, and the estimated cost there is 82,705. Then she sets out if all home treatment patients were to be included what the total requirements would be.

Then if we look in the next paragraph, there's a recommendation about central purchase. Then doubts were expressed about the fairness of allocation of Lister concentrate between regions because of differences in severity of patients.

Do you know what that refers to?

A. I'm not sure about the issue of the differences in severity of patients in regions, but I think Mark Winter mentioned that you got back what you put in, to some extent, and so if you had a region where you had plenty of donors, you tended to get more concentrate back. Whether that was equitable or not is another matter altogether. But I am not familiar with any particular relationship between the allocation of Lister concentrate and severity of patients.

Q. If we move on to a later meeting in 1978. Henry, it's BART0000686, please. This is a meeting of the same

working party, 29 November 1978. We can see that you're present, as is Dr Kernoff. If we go down towards the bottom of that page, we see under the heading "Central funding of commercial Factor VIII concentrate purchase" there's a suggestion there of central funding of commercial Factor VIII concentrate purchase for the NETR, (the North East Thames region).

Can you recall why that was being recommended?

A. I can't, although I have seen other correspondence you have provided for me on the subject. I think that the issue really is that if you have lots of little centres buying concentrate separately, they tend to have to pay more per unit than if you have a bulk purchase. I think Mark Winter mentioned this himself.

The other concern, of course, is that if there are centres buying their own concentrate, you don't know what they are doing with it. If you've got a central purchasing system and if the commercial concentrate you have delivered is delivered centrally to either the Royal Free or The Royal London, you've got some sort of control over what happens to it. We were talking earlier about the autonomy of the peripheral centres, and they were autonomous. They could do what they liked, but they also appreciated

the advice they got, I think, from the centre, and so the co-ordination would work better and more economically if there was a regional policy on factor purchase.

Q. If we go to the next page, please, Henry, we can see that expressed at the top of the page is an aim for BPL to be able to supply all the Factor VIII concentrate required for the region.

Then if we go down, please, Henry, to the third paragraph, you are recorded there as pointing out that:

"Many home treatment patients were still on cryoprecipitate and that considerably more commercial Factor VIII concentrate was needed than used at present."

Why was it that more commercial Factor VIII concentrate was being identified there, bearing in mind your policy, as I understand it, was that home-treated patients would receive NHS factor concentrate?

A. Only that we didn't have enough NHS concentrate for our purposes. Obviously, we moved fairly soon after that, I think, to cryoprecipitate being replaced by factor concentrates in the community, and all I think I was trying to say, though perhaps it hasn't been

very well put in the minute, was that if we weren't going to get NHS, we needed commercial concentrate.

Q. I'll come back in a few minutes, if I may, Dr Colvin, to the question of continuing with cryoprecipitate.

A. Sure.

Q. But still with this document, if we go to the next page, we can see the top of the next page, Dr Lane there identifies three lines down:

"Supply of NHS factor concentrate is inadequate at present for two reasons."

The first reason he gave was substantial underinvestment in BPL.

Was that a concern that you and your colleagues shared?

A. Well, I think we all had that feeling. I mean, I remember going when I was a very young doctor up to visit Darcy Maycock in Elstree, I think it was, and I mean, I could see that this wasn't a terribly professional organisation in a way. I mean, it was part of the NHS but not locked into the NHS because it was the Lister Institute I think.

So I think that the feeling was that the commercial companies, particularly in America of course, were a bit ahead of BPL technically and in the capacity to produce the concentrate. David Owen was

clear about this himself. He realised that there needed to be investment in the preparation of concentrates in order to make us in any way self-sufficient.

The sort of principle of making concentrate is actually rather straightforward. You just take your plasma off the red cells by centrifugation, then you freeze it, then you thaw it, and you thaw it at temperature of 4 degrees Celsius so you can just lift off the cryoprecipitate. Then with the cryoprecipitate, you start using the fractionation process that was invented during the Second World War to create the lyophilised freeze-dried powder concentrate. So it's not fantastically complex in theory or perhaps in practice, but it needs to be done on an industrial scale. You can't do it with a very small organisation or a very small factory. It's a factory process. It's not a simple process like making cryoprecipitate.

Q. Then the second concern there identified by Dr Lane is:

"Insufficient supply of fresh frozen plasma from Regional Transfusion Centres, coupled with the use of 5L plasma pooling providing source material of low potential yield."

Was that a concern that you and your colleagues shared?

A. Well, I think the insufficient supply of FFP is obviously the source material. So if you haven't got enough plasma, you haven't got enough concentrate. It makes perfect sense.

The use of the plasma pooling process, I'm not quite sure what that means, but it is important to appreciate that every step you make in fractionation results in a loss of yield. So if you start with 100 units, say, in your plasma, by the time you get to your cryoprecipitate, you have perhaps lost 10 per cent. Then you get back to your concentrate, you have even lost more. If and when you get around to viral activation, you are going to lose also concentrate in the viral activation process so that if and when you decide on the capacity of the viral activation, you're going to have to have more plasma to produce the same amount of concentrate.

Q. Then just if we go over the page, please, Henry, the bottom of the next page, we can see the last paragraph says:

"Dr Jenkins was concerned about the possible increase of Australia antigen positivity in home treatment patients and their families. It was agreed

to ask Sister Mary George to look into this, with a full report and discussion at the next meeting."

Do you have any recollection as to what that particular concern was?

A. No. I suspect -- I mean, John Jenkins was a great man, but he was of another generation, and maybe when he was talking about Australia antigen positivity in home treatment patients, he was thinking about the past when hepatitis B, that is Australia antigen, had been a big problem. But by the time I qualified, and by the time I started practising haematology, hepatitis B -- although I had patients who had hepatitis B positive -- was not a big problem for the future. It's even conceivable that John Jenkins was actually worrying about non-A, non-B, rather than Australia antigen. But it is quite difficult to understand what that meant.

Q. Could we then go, Henry, to BART0002487. This is the letter we looked at briefly earlier from Dr Kernoff to you, 27 April 1979. I just want to look at some other parts of it now, please. If we go down to the second main paragraph, please, Henry, you'll see set out in the second main paragraph Dr Kernoff saying:

"The regional treasurer has recently refused our request to institute a system of central funding for

Factor VIII."

Then there's a compromised proposal and view set out there. Halfway down this paragraph, it says this:

"It is also felt that there is a lack of understanding at regional level of the special problems of treating haemophiliacs and, in particular, the problem of obtaining adequate supplies of Factor VIII. This problem will not be solved by stop-gap measures and will be with us for at least several years to come."

Do you know what was meant there by a lack of understanding at regional level of the special problems of treating haemophiliacs?

A. I think Mark Winter really touched on this quite a lot in his discussion, and he said that haemophilia was a low-volume, high-cost condition which required a lot of investment for a rather small number of people, and of course that's true.

I think that region didn't necessarily understand how difficult haemophilia was. This brings us back to what Mark was saying of how awful it was to have haemophilia without any treatment and that at regional level, I'm sure they were thinking about, you know, as we do today, about heart disease and cancer affecting the population at large, and they may have

felt, well, what is this about?

It is quite technical. The business of how to treat people with haemophilia is relatively technical, and maybe there just wasn't an understanding of what the real problems were for a person with haemophilia, and what the potential solutions were, and how important it was to address them.

Q. Dr Winter's evidence in that regard suggested that there was, at an institutional Health Service level, perhaps a lack of priority accorded to haemophilia in terms of funding allocation. Was that your experience?

A. I think that's entirely possible. Don't forget, certainly at this time -- at this time, there were perhaps 5,000 people with haemophilia in the United Kingdom -- A -- a thousand or a little bit less a thousand of people with haemophilia B in the United Kingdom. We were looking at about 6,000 people in a population of 60 million. Those 6,000-odd people clearly were extremely important, and I spent the whole of my career trying to look after a small number of them. But you can see that if you were running the NHS or the region, you might say, wrongly, who are these 5,000 people? Why are we having to spend so much money on them? That's the kind of

atmosphere maybe might have been around.

Q. If we go on to the next page, please, we can see -- this is the passage we looked at earlier under the heading "Types of therapeutic material available", and then reference made four lines down:

"Three Factor VIII-containing preparations available: cryoprecipitate, semi-purified Factor VIII concentrate made by the NHS, and semi-purified Factor VIII concentrate made by commercial companies. Cryoprecipitate, although relatively cheap to produce, has clinical disadvantages."

I am going to come on to those what you might say the disadvantages were:

"And in the UK, as in all developed countries, is being superseded by semi-purified Factor VIII concentrates. Since the amount of concentrate being made by the NHS is at present quite inadequate to satisfy needs, the shortfall has to be met by buying commercial concentrate."

Then it goes on to consider the issue we looked at earlier.

What appears to be being set out here is a policy, a way of thinking, which is: cryoprecipitate is the past.

A. Mm-hm.

Q. Concentrates are the present and future. There isn't enough NHS and, therefore, the only answer is to buy commercial concentrate.

Would you agree? That's a precis.

A. Absolutely fair.

Q. What consideration was given within the North East Thames region to, rather than making up the shortfall with commercial concentrates, making up the shortfall at least to an extent with cryoprecipitate?

A. Well, now we come down to the issue of: what is cryoprecipitate; what's it useful for, and how does it work?

So cryoprecipitate, as I've explained, is very easily produced from a bag of blood. You just freeze the plasma, thaw it at 4 degrees, take off the supernatant and refreeze. Each bag contains 1 unit of another person's blood, and you store the cryoprecipitate in a deep freeze. You have no idea how much Factor VIII is in it because there's no way of measuring it, and it's full of everything else. Admittedly, it hasn't got the red cells but it hasn't got the supernatant, but it's full of fibrinogen and Factor XIII and globulins and all sorts of stuff. It's very impure. It's also full of allergens, that is things that can create allergy.

So when you're using cryoprecipitate, you have a large volume, perhaps only concentrated by a factor of 10 from the plasma itself. You have the likelihood of severe side effects. Okay, you can get minor allergic reactions, but they can be extremely severe and could potentially be fatal. You don't know how much factor is actually in the bag you're giving, and it's extremely inconvenient to make up. So that if you are trying to -- if you are a junior doctor in the middle of the night and you are not in the haemophilia centre because, you know, people go home, you will have a young doctor who's got to make up 10 even possibly 20 bags of cryoprecipitate in the middle of the night because the half-life of Factor VIII is only 8 to 12 hours, so you can't go home and then not give any more until tomorrow morning if you've got a seriously affected patient.

It becomes quite impossible to use it in an effective way and in a reliable way when you've got an alternative that is easy to use with a known volume of Factor VIII in it and with a limited immediate side effect which is extremely attractive to use. You heard patients talking about this on film, saying their lives had been completely transformed by the concentrate.

Now, the next thing you ask me is, well, you were able to give cryoprecipitate in the home. Why couldn't anybody else? The answer is: people could but it was very unattractive. You had to have the freezer, you had to have much bigger surface on which to make up the material, you had to worry about the allergic reaction, and you didn't know how much to give.

So I think we did give up on cryoprecipitate because -- not just because it was inconvenient, but because it wasn't as reliable, and it was more dangerous at an immediate allergic level.

Q. Can we just unpick some of those issues, Dr Colvin?

First of all, just dealing with the potential to give rise to an allergic reaction.

A. Yes.

Q. Is there any data on how common that was?

A. I'm not sure about scientific data, but if you look through -- as I recall, looking through my notes, I would often find that the person was known to be allergic to cryoprecipitate. It was extremely common. Of course, the level of allergy -- that is the seriousness of the allergic response -- varied from person to person. But I think there was a lot of reluctance to submit patients to what, at best, was an

unpleasant experience and what, at worst, could be a very serious experience once they had experienced it. So it wasn't just an excuse. It was a reason for not giving cryoprecipitate. First, they had an allergic reaction, then I think it was time to move to concentrate.

Q. But in terms of maybe the scientific data that you are able to point to -- in terms your own clinical experience, very approximately to give us an idea, what proportion of patients on cryoprecipitate experienced a significant allergic reaction?

A. A third to a half. It's hard to say, but I think at least a third.

Q. You have also in your witness statement, where you have listed a number of disadvantages to cryoprecipitate, suggested that it was impossible to sustain in home treatment, and I want to suggest to you "impossible" might be overstating the position.

A. Well, I mean, you might say nothing is impossible. Maybe the word "impossible" is too great since I use it in home treatment. But I think it was impossible to sustain in the light of the advances that had been made in haemophilia care, and I don't think it was realistic to continue cryoprecipitate use in the home. It wasn't fair to the patients, and it wasn't the

right thing to do.

Q. There are -- practically it takes longer --

A. Yes.

Q. -- and a freezer is required, but we're talking about an ordinary, domestic freezer. We're not talking about some special piece of scientific equipment?

A. No.

Q. We know that it was done at the Royal Free, in particular, under Dr Katharine Dormandy quite extensively in the course of the 1970s.

A. Yes, sure.

Q. The Inquiry has heard evidence from others in other parts of the country who were treated with cryoprecipitate in the 1970s.

I don't doubt that concentrates may have been more convenient, may have been quicker, but would you accept that those advantages would have to be balanced against risks, in terms of viral transmission?

A. Advantages always have to be balanced against disadvantages. It's quite right and, of course, it is the case that I used cryoprecipitate myself in home treatment. I wouldn't begin to deny it. I'm delighted to do so, to begin with, because it made such a big difference.

But I don't know how long the Royal Free went on

giving cryoprecipitate to patients for home treatment. Maybe Professor Lee can tell you, although she wasn't perhaps there at the time when that decision was made. But I think you'd find that, throughout the United Kingdom, and probably throughout the developed world, people were "giving up" on cryoprecipitate to use concentrates. The analysis of the advantages and disadvantages at that time, in our view, in our world was that it was time to move on to cryoprecipitate -- from cryoprecipitate to concentrate.

Q. All things being equal, if there were no difference in the risk of viral transmission, as between cryoprecipitate and concentrates, the clinicians' preferences for concentrates, or indeed the patients' preference for concentrate, may be entirely explicable for the reasons you have given. But wasn't the risk of viral transmission the elephant in the room; the factor you couldn't ignore in deciding whether to abandon cryoprecipitate or not?

A. Well, let's move on now to look at the risks of cryoprecipitate. If it is the case that the prevalence of hepatitis C in the British community is let's take the figure 0.3 per cent, that's 3 per thousand, if you use potentially 10 bags of cryoprecipitate for your treatment and if you might

treat yourself two or three times a week, that would give you, I think, shall we say, up to 100 bags a month. I mean, I'm just -- I'm not doing the maths particularly now, but, I mean, you can see, it doesn't take long to build up a very large number of bags of cryoprecipitate.

Now, you might, of course, get the same person giving to the bag. So if you've got the same person giving to bags as time goes by, you are not exposing yourself to a new donor every time you get a new bag of cryoprecipitate. But it doesn't take long for you to get into the thousands of bags of cryoprecipitate.Then, of course, it is a matter of risk analysis. But you're really playing Russian roulette with a machine gun, that eventually if you have enough bullets one of them is going to hit you.

So, in that sense, with respect, in the end you're going to get hepatitis C.

Q. Let's look at it in a slightly different way. We haven't come on to talk about HIV yet because I'm asking you these questions in a chronological order largely, but would you accept that the risk of being infected with HIV from cryoprecipitate was far, far -- you couldn't say it was non-existent but far, far, far smaller than the risk of being infected with HIV

through concentrates?

A. Yes, of course.

Q. In relation to hepatitis, you may be right to say that you can't say that there is no risk of infection with hepatitis from cryoprecipitate, particularly if you are someone who is using cryoprecipitate a lot, but of course not every haemophilia sufferer would necessarily have been using cryoprecipitate in a way that builds that up?

A. I agree.

Q. We can put lots of different numbers into each side of the equation but would you agree that cryoprecipitate carried a lesser risk, didn't carry with it the certainty of infection with hepatitis C that you have pointed to in relation to concentrates?

A. I understand that. There's one other point I would make, though, and that is if you did get a bag of cryoprecipitate that was infected you could get a big dose of virus and could be quite ill.

There's a paper published by Peter Carr, from Christine Lee actually -- and she can refer to it, I'm sure, when she gives evidence -- where they specifically reported in Gart(?) a patient who was given a dose of cryoprecipitate who was extremely unwell.

So it's very important not to take the view -- I know you don't take the view -- that there's no risk giving cryoprecipitate. It's not the case.

Q. What I'm seeking to explore with you, Dr Colvin, is when we look at, for example, this document, and we'll see it and a handful of further minutes in a moment, what we don't see is that risk analysis being undertaken, at least not expressly?

A. Yes.

Q. No-one appears to be asking themselves the question: what are the relative risks of cryoprecipitate and factor concentrates whether NHS or commercial?

A. Yes.

Q. Is that fair? That wasn't something that was expressly considered at that time?

A. I think it's fair to say that we didn't expressly consider the possibility of going backwards to cryoprecipitate use in a big way.

Q. Do you think the reason for that may have been in part what Dr Winter alluded to and what you alluded to yourself, a sense of wishful thinking and everything -- liking so much the effect of concentrates on the lives of your haemophiliac patients, you didn't want to think about going back?

A. I'm sure that's true. The other thing, of course, is that if you had decided that cryoprecipitate was the answer, which it certainly was not, then what happens to the fractionation unit? Do you give up the idea of fractionated concentrates and freeze-dried concentrates?

I think that there was a sense, and a true sense, in which cryoprecipitate was old hat. I take your point about the risk, and I think if you come on to some of the things I tried to do, you'll see that I was still using cryoprecipitate in certain circumstances, but in very, very selected circumstances, and that none of us really contemplated a return to cryoprecipitate as the first line of therapy.

Q. Just going back to this letter, if we could go to the next page please, Henry, and just really to complete the factual position, we can see from the heading, "Financial arrangements", picking it up third line down:

"NHS-produced cryoprecipitate and Factor VIII concentrate are distributed without charge to Haemophilia Centres in NETR ... either at Brentwood or Edgware ..."

So you were, as a matter of fact, able to get

both cryoprecipitate and NHS Factor VIII without having to pay for it from --

A. Yes, indeed.

Q. Then if we go to the next paragraph, please.

If we just look towards the bottom of that next paragraph, there's a sentence -- if you need to read the whole paragraph, Dr Colvin, do, but there's a sentence beginning:

"Directors of these Centres ..."

This was the smaller centres:

"... have had considerable difficulties persuading their local administrations to purchase factor VIII."

That's commercial Factor VIII?

A. Yes.

Q. "I know of no other instance where supplies of an essential drug have been withheld on the grounds of cost and in my view the refusal of local administrators to purchase commercial Factor VIII is a serious interference with the duties and rights of physicians to treat their patients in the most appropriate way they think fit."

I wanted to ask you about that latter sentence there. Is this the concept of clinical freedom that other witnesses have referred to?

A. I don't think it's to do with clinical freedom. You say -- are you trying to now refer to the "I know of no other instance" paragraph?

Q. Yes.

"... serious interference with the duties and rights of physicians to treat their patients in the most appropriate way they think fit."

A. I mean, this is an anecdote, from my experience.

Years ago I was asked, as we were trying to get funds for haemophilia care, for how long haemophilia had been treated at The London Hospital. As it happened, I knew that Sir Frederick Treves, in the late 19th century, had looked after a family of people with haemophilia and had published in The Lancet. So I was able to tell my district treasurer, who was saying to himself, really, "Why should I be doing this?" that we had been treating patients with haemophilia at The London since the 19th century.

I think he rather -- he thought he was joking, but he wasn't, he said, "Well, perhaps Dr Colvin could treat all his patients for half the time or half his patients for all the time."

I mean, that's a damning remark, I think you will agree, which is not far away from this statement, and was utterly unacceptable to anybody who was

a healthcare practitioner. So in that sense, it is true that district treasurers were very unhappy about the idea that they had to spend money.

It's also important to appreciate, and we go back to the earlier part of the paragraph, that you have said that the cryoprecipitate and the NHS concentrate was a free good, which of course it wasn't, because it had to be paid for by the NHS. But we know the NHS is free at the point of delivery -- thank heavens because the whole of my career was based on having the ability to give people of any social class exactly the same treatment -- enormous benefit for the whole of our community, which we've celebrated for all the years since '48. But the commercial concentrates had to be paid for with real money.

Now as we moved on and it became apparent that NHS concentrate was going to get really expensive, because it became more and more difficult to produce it, because it was getting purer and purer -- the actual use of the fractionation industry got more and more complex -- so it became more and more expensive to make the product we required. That's when the idea of internal charging was introduced, with the idea of trying to make some sort of sense of the relationship between the NHS as a provider where treatment is free

at the point of delivery, and the whole system works in that way, and the import of commercial concentrates that had to be paid for.

You will recall that during Mrs Thatcher's premiership she described -- I think I'm just about quoting -- the NHS is not a business run for profit but it can be made more business-like. That's what she said at the NHS review in her premiership.

That was, in a sense, what was happening at these times, that it was recognised that something had to be done to make the haemophilia service work at a financial level. That's what I think these treasurers were trying to achieve, albeit sometimes with language which was unacceptable, and with a policy which was not acceptable to us as clinicians.

Q. Could we then go on to one further set of minutes from 1979.

Henry, it's BART0000683.

You can see this is a set of minutes from 1 August 1979. Again, you and Dr Kernoff and others are present. If we go down towards the bottom of the page, please, under the heading "Matters arising from the minutes", the last paragraph says this:

"In the meantime Dr Carmichael stressed that the Haemophilia Centres must demonstrate the best use of

available resources. In the present financial situation, there could be no point in competing with other medical groups equally stressed by shortage of funds. He repeated that 'good housekeeping', active decisions when not to treat patients, using cryoprecipitate where ever possible, and cutting out expensive elective surgery, for example remedial orthopaedic surgery, would all demonstrate a careful and responsible use of available funds."

Now those are measures that are being suggested on financial grounds. But they are all measures which might have had an impact in terms of reducing risks of viral transmission. There's --

A. But I think you have to understand -- sorry, I --

Q. No, no, please comment.

A. I think that the difficulty, therefore, is to contrast the prudent, if you like, use of resources trying to provide a high quality service and the profligate use of resources trying to provide a high quality of service. There were people in the United Kingdom in haemophilia centres who really didn't care, I think, what it cost and who believed that the more concentrate you used the better, and they may have been right.

You'll realise that the Germans, for instance,

were using enormous quantities of Factor VIII (particularly perhaps Dr Brachmann in Bonn) and I think many people thought that, and in many ways they were right, that we should be doing everything we possibly could to make haemophilia care perfect and that meant using a lot of Factor VIII concentrate.

Other people thought: Well, I'm not sure that's necessarily the best strategy. If you look at the usage figures, which I have and you have provided for me, it looks as though, at The London, we were using possibly about half the amount per person with haemophilia as was being used nationally.

Now, why was that? It might have been because I had lots of mildly affected patients. Maybe that was part of the reason. But it might have been that I was trying to be a good housekeeper. On the other hand and this has been said to me by at least one director in the past, "Brian, you should be using much more concentrate and you are letting your patients down by not using higher volumes". My view was that I wasn't letting my patients down, that I was giving them the appropriate treatment, but nevertheless in the context of good housekeeping.

But I don't believe what Dr Carmichael said was right at all.

Q. So would it follow from what you've just said that you yourself did not, whether for financial or risk-based or other reasons, implement the measures that he set out here?

A. I don't think I should have done.

Q. Then if we go over the page, we can see you saying in the second paragraph and this is in the context of a discussion about limitations of funding:

"Dr Colvin reported that he would be forced into clinical decisions which no-one would wish to make. There were genuine fears that patients would die due to lack of treatment. The first sufferers would be patients requiring remedial surgery, hip replacement or repair operations, et cetera. If not offered surgery, such patients would remain a drain on available resources ..."

Et cetera, et cetera.

Then the next paragraph:

"After further discussion [it] was agreed to conserve available Factor VIII resources as carefully as possible and to encourage the expansion of the Blood Products Laboratory, Elstree ..."

We can see therefore what your concerns were, Dr Colvin. What do you understand that meant by the agreement in the next paragraph to conserve available

Factor VIII resources as carefully as possible?
A. It is always, for any physician, the duty to conserve available resources within a proper use of those resources. So, as you will have seen from my CV, I was also Associate Medical Director. Now, I remember having another conversation with one of my colleagues who said, "What are you doing being Associate Medical Director at the same time as being a haemophilia doctor? You should be fighting your patients' corner, not thinking about your relationship with the hospital as a whole and being interested in the allocation of resources."

Well, I can't really agree with that thesis. If we all -- I can see the idea that one should be fighting one's patients' corner, I tried to do that throughout my career, but it is essential that there's an organisation and that resources are allocated. It's a fact of life that the resources are not infinite and have to be allocated.

So nobody should argue with the statement it was agreed to conserve available Factor VIII resources as carefully as possible. That's good housekeeping. What is not acceptable is to say that you're not going to be bothered with remedial surgery and people's pain and suffering when you know that remedial surgery will

make the patient's condition better and will enable them to go back to work and be out of pain.

So this is an ancient, no doubt, dilemma and it's with us today.
Q. If we go down to the bottom of the page we can see the policy that appears to be agreed, but agreed on financial grounds rather than anything else. Point 2:

"That all NHS Factor VIII concentrate should be allotted to Home Treatment patients as a first priority, and that the presently available 370 bottles of Factor VIII concentrate per month should be allocated to the London and Royal Free hospitals in proportion to the numbers of Home Treatment patients at each Centre."
A. That sounds like good housekeeping to me.
Q. So would it follow from that -- it picks up on what we were talking before lunch, Dr Colvin -- that in relation to those who were not on home treatment, commercial concentrates would now increasingly be filling that gap?
A. Well, it depends on what's to be done. It's not sensible I think and I don't think we did devote all of our NHS treatment to home treatment. There was some NHS treatment available. We didn't spend all our hospital treatment or all our surgical treatment on

commercial products. By no means. But it was inevitable that if you had a big procedure then it might need to require commercial product.
Q. If we go to the next page, paragraph 3, top of the page, it's then said, and this is part of, again, what is recorded as agreement:

"Wherever possible, Hospital patients (including out-patients visiting for treatment) should be treated with cryoprecipitate or Commercial Factor VIII concentrate, the exception being Home Treatment patients previously exclusively treated with ... Factor VIII concentrate."

So there doesn't appear to be any suggestion in this meeting that cryoprecipitate is somehow inherently not to be favoured or disadvantageous?
A. No, I think that there was no reason why cryoprecipitate should not be used in occasional circumstances, and I can show that I was doing that, for instance, for very small children or -- until the mid-80s. There were still patients I was treating with cryoprecipitate.
Q. Then if we go, please, to BART0000681.

We move forward here to a meeting in April of 1981 of the same working party. We can see again that you are there and Dr Kernoff is there.

If we go down towards the bottom half of the page, please, we can see in the penultimate paragraph:

"It was agreed that all available NHS Factor VIII concentrate should be allocated to patients on Home Treatment ..."

So the same policy still seems to be applied in April 1981.

Then in the next paragraph we see, last five lines:

"In-patients who require prolonged or intensive treatment should receive cryoprecipitate or commercial Factor VIII concentrate."

Just pausing there, again, there doesn't seem to be any suggestion that cryoprecipitate is inappropriate or unsuitable for prolonged or intensive treatment.
A. But it doesn't say anything other than the fact that one could consider using cryoprecipitate. It doesn't mean to say that cryoprecipitate is suitable for all intensive treatment. It isn't.
Q. No, but there is nothing in here to suggest that it's inherently unsuitable?
A. No, and I think -- I mean, I don't know if and when you want to discuss the very small paper I wrote in the 80s but I made quite clear that I was still

selecting people to receive cryoprecipitate into the '85 period.

Q. I will come to that when we get on to the mid-80s after we have looked at HIV.

Then you refer there to:

"... young children who react to cryoprecipitate may receive ... Factor VIII concentrate ..."

If we just go over the page, we can see this it says:

"Brentwood Regional Transfusion Centre wishes to decrease production of cryoprecipitate so that more of the available plasma can be sent to the Blood Products Laboratory, Elstree, as Fresh Frozen Plasma. Brentwood would continue to produce some cryoprecipitate and would be prepared to set aside cryoprecipitate on request for planned cases. Centres should be prepared to use commercial Factor VIII concentrate for in-patients ... in place of cryoprecipitate."

Something of a tension between the suggestion on the previous page that in-patients should receive cryoprecipitate or commercial Factor VIII but here we're seeing a suggestion of a reduced production of cryoprecipitate. Do you recall any discussion about that issue?

A. I don't recall that particularly but I think that the -- I've been listening and watching for some days, and I think there's a sense in which, for perfectly understandable reasons, the Inquiry is -- are unable and unwilling, I think -- I perfectly understand this -- to realise that the haemophilia treaters felt, rightly or wrongly, that cryoprecipitate was a treatment of the past, that it was low tech, if you like, and that it would be replaced, in its entirety really, by concentrate. That eventually of course happened when effective virally-activated concentrates became available. So we are looking at 1988 really that -- that's the end of cryoprecipitate as a realistic treatment for haemophilia.

But in this period in the late 70s, it nevertheless was the case that people felt, rightly or wrongly, and with some clarity, that the days of cryoprecipitate were over. Not just because of convenience but because it wasn't a good way of treating haemophilia.

Q. Dr Colvin, it is clear that some people thought that. The question I'm seeking to explore with you is where into that decision-making process did an analysis of risk come? I think earlier you agreed with me it didn't really feature.

A. No, I think that is fair, that because of the lack of engagement on the non-A, non-B risk of factor concentrate, the potential advantage of cryoprecipitate for relatively infrequently treated patients with haemophilia might not have been addressed properly.

Q. I suggest to you that's something that one can say not just with the benefit of hindsight but, looking at things at the time, there should at least have been an evaluation of the relative risks as part of the decision-making process?

A. Well, what is and is not hindsight I can't judge, I guess that's for Sir Brian to judge, but I think that it is with hindsight that we appreciate that more attention should have been made to the potential of cryoprecipitate.

Q. Can I just go back to the question of DDAVP, which we were talking about before lunch, and just ask you to look at a couple of documents in relation to DDAVP.

Could we please have, Henry, MASK0000605_002.

We can see that this is a report in The Lancet from 1 October 1983 entitled "DDAVP in Haemophilia and von Willebrand's Disease". Picking it up towards the bottom of the left-hand column it said:

"For its ability [so that's DDAVP's ability] to

raise the plasma concentration of Factor VIII, it is finding an increasing place in the treatment of haemophilia. In mild haemophilia A and von Willebrand's disease ... excessive bleeding usually occurs after trauma or surgery and can be effectively treated by cryoprecipitate or Factor VIII concentrate. The use of blood products, however, is not without dangers. Even with a modest number of factor VIII infusions, many patients or infected with hepatitis B or non-A, non-B and these infections may well progress to chronic active hepatitis and cirrhosis. If it renders transfusion unnecessary in selected patients, DDAVP therapy must be counted an important therapeutic advance."

Is then if we just go to the next page, and then I'll ask you about it, Dr Colvin. So left-hand column please, Henry:

"DDAVP can be used to treat patients with mild haemophilia, carriers of haemophilia with low Factor VIII concentrations, and patients with [von Willebrand disease]."

Then it goes on to describe how it will be given and what its effect is. Then, if we can pick it up a few lines down:

"Provided that the basal level of the most

deficient Factor VIII activity ... is 7 per cent or more, the resultant rise, which reaches a maximum within 60 to 120 [minutes], should be sufficient to stop external haemorrhage ... or to allow minor surgery such as tooth extraction or lymph node biopsy."

Pausing there, that, I think, is essentially the observation you were making earlier about your usage of DDAVP. Then it goes on to say, if we skip over a sentence:

"Bigger surgical procedures [and a couple of examples are given] ... may be possible with DDAVP if the basal factor VIII levels or higher, particularly in [von Willebrand's disease] ... A further injection of DDAVP can be given after a few hours to boost the Factor VIII concentration ..."

And so on, and it talks about different ways in which the DDAVP can be administered.

So it would seem there, in 1983, it's being suggested that DDAVP isn't necessarily limited to the more minor forms of surgery that you referred to.

A. First of all, we don't know who wrote The Lancet article, because Lancet articles are always anonymous. Secondly, I can share with you my own view of the value of DDAVP, which is not the same as this. I am

happy to explain that to you.

So I have used a very large amount of DDAVP and tranexamic acid in my time, and I think that's demonstrable from my returns. It's an extremely valuable treatment and it's very useful in people who have Factor VIII levels of around 5 to 10 per cent, because you get a three to five-fold increase.

So if your resting level is 5 per cent, you'll get up to maybe, if you're lucky, 20 per cent. That's not a very good level but it might give you haemostasis or it might not.

Therefore, one links it with a drug called tranexamic acid, which has become rather popular these days, and it's often in the press, and tranexamic acid helps prevent the dissolution of blood clots. So the idea is that if you give a dose of DDAVP and tranexamic acid you'll just about get a clot formed and tranexamic acid itself may just about prevent that clot from dissolving before you start bleeding again.

Now, DDAVP, as I explained earlier in this discussion, is affected by a process called tachyphylaxis, and that process of tachyphylaxis means that DDAVP is delivering what you've got inside your body to your circulation. If you give it every 12 hours or so, by the third dose you will have run

out of your own resources. So it's no good for more than two or three doses because it -- you lose the effect.

So if you've got a simple small dental extraction, give the DDAVP and tranexamic acid, perhaps give another dose and wait and hope that everything's fine, you're okay. But if you try to do that when there's a risk of a haematoma forming, as I explained this morning, you may actually do more harm than good, because you're left with a haematoma which you then have to try to resolve, which may take days or weeks to resolve.

So also I pointed out some patients with von Willebrand's disease are not suitable for DDAVP, particularly types 2B and 3, and that means that I have to work in my own mind when it's suitable and when it's not. Here it says you can do a cholecystectomy or a thoracotomy under DDAVP. I completely disagree. I think it is a very foolish thing to do. Personally. But as we discussed before, there is this thing called clinical freedom and different people have different views.

But I do emphasise that I'm a great enthusiast of DDAVP but only in certain selected circumstances, and I think my own use of DDAVP is more conservative

than is expressed here, for the reasons I've given.

Also, DDAVP retains fluid because it's a brain hormone which is fluid-retaining, and is therefore unsuitable for neonates and, if you repeatedly give it, having run out of your effect of stimulating Factor VIII production, then you could cause fluid retention which could be harmful. Also, of course, it's completely useless for managing haemophilia B. It doesn't work.

Q. I think the answer to this next question may be obvious from what you have just said, Dr Colvin, but did you yourself ever use or recommend DDAVP for bigger surgical procedures than the ones you have described?

A. No.

Q. Could I then just ask you some broader questions about your approach to treatment.

We know you had a policy for how children would be treated predominantly but not exclusively with concentrates. What age of children did that policy encompass?

A. Well, I think, as far as the use of cryoprecipitate in the children's ward, it would have been rather young children because once people were going to grow up, they tend to get on to the home treatment programme,

and then they were on concentrate. So what I'm thinking about really was very small children. There's one case that -- obviously, it's difficult to talk about individual cases, but there was one child who was referred to us I think in the early '80s from Great Ormond Street, and we carried on with cryoprecipitate until the -- sort of '85 or so, '86, maybe '87 when what 8Y came in, and he avoided all virus infections because we had insisted on his having cryoprecipitate when he was a little child as an in-patient in the hospital.

But that only -- that sort of happy outcome was really quite rare for the reasons that I expressed in my --

Q. Just, as a matter of fact, what age of children? You said it was the younger children. Are we talking under 6? Under 10?

A. I think probably more under 6 than under 10 because I think once you get to a bigger, substantial child we'd have had them on the home treatment programme, if we could.

Q. And, thus, concentrate --

A. Yes.

Q. -- preferably NHS but in some circumstances for supply reasons --

A. Yes, and paradoxically, if you were a child who lived near The London and were perhaps socially deprived and weren't suitable for the home treatment programme, you modified be less likely to go on to the home treatment programme, therefore more likely to be treated with cryoprecipitate.

Q. Then I think as you told the Lindsay Tribunal, although there was this policy in relation to the treatment of children, as a matter of fact, you didn't have a particular policy for the treatment of previously untreated patients.

A. I don't think the policy -- since most of the previously untreated patients would be very small children, the policy would have been to use cryoprecipitate. So maybe I didn't have a specific policy at that time for the treatment of previously untreated patients, but I think the effect of the policy we had would be that they would be given cryoprecipitate.

Q. In your witness statement, you say that the reason for trying to reserve NHS Factor VIII for children not on cryoprecipitate or for home treatment was partly safety, and I wondered if you could just expand on what you mean by "partly safety"?

A. Well, only that I think that at the time I took the

erroneous view that the NHS concentrates had the lower risk of causing hepatitis than the commercial concentrate. I was wrong, but I think that that would have been the reason that I would have thought in those terms.

Q. Then if you wouldn't mind turning up your witness statement, Dr Colvin, and going to paragraph 15, you list in paragraph 15 a number of different products that were used over the years at The London Hospital for the treatment of haemophilia A and B.

I wondered if you could just assist me with -- in fact, maybe we'll put this up on screen. It might be easier to follow. Henry, it's WITN3343007.

If we go to page 7, and we'll see bottom half of the page, you have listed a number of products. Could you assist me with an exercise of just ordering those products by reference to safety considerations alone, where -- obviously, these are all products available at different times. They are not simultaneously available to you, certainly not in the late '70s and early '80s. If we leave aside recombinant on the basis that presumably in terms of viral transmission that is the safest, albeit in its initial form not 100 per cent safe, and I will be asking you tomorrow a little bit more about recombinant.

In terms of safety, and I'm talking here about viral transmission not possible allergic reactions, so it's a limited question.

A. Yes.

Q. What is the safest of those products in your view?

A. From the point of view of viral transmission?

Q. In relation to viral transmission.

A. Obviously, desmopressin.

Q. Then after that?

A. Well, if you're talking about human infection, then I suppose the answer's probably porcine Factor VIII. The trouble with porcine Factor VIII was that it was withdrawn because of potential contamination with porcine parvovirus. So there's a kind of bracket around that really.

If you then go on, the fresh frozen plasma and cryoprecipitate are of equal risk, except insofar as you couldn't give enough fresh frozen plasma to reach the same number of units as you would use for the same volume as cryoprecipitate.

Then the next most -- the next safest would be the NHS Factor VIII heat-treated after 1988.

Q. Yes. So that would be 8Y?

A. Yes. Then -- are we only talking about Factor VIII now, or are we talking about Factor IX as well?

Q. By all means, talk about Factor IX as well.
A. I think the Factor IX heat-treated after 1985 was demonstrably safe in the same way as 8Y was.

Then probably Factor IX unheated because -- I'm sorry. We're on to virally -- I've got to go down to virally inactivated, haven't I? The next thing is virally inactivated concentrates. That would have been the NHS virally inactivated 8Y or 9A.
Q. Yes.
A. After that, we are in a degree of difficulty because the NHS Factor VIII really was an unknown quantity until we got to the 8Y because there was very small amounts of it. It's hard to interpret, which you may come on to later.

Then I think of the -- if you're talking about hepatitis C and HIV together, which is quite difficult because they have slightly different levels of safety, the heated commercial concentrates whether 8 or 9, were very capable of transmitting both HIV and HCV. Eventually it perhaps was clear that the heated commercial concentrates had some benefit to begin with; it's difficult to be sure. Then I think the Factor IX commercial, I think we didn't have enough information really to judge.

Then I think, equally, probably the Factor VIII

Inhibitor Bypassing Fraction that was heat-treated would have been much the same as the other commercial heat-treated. Then I think you'll see from the papers we've got that in the end it became clear that the commercial concentrates that were not heat treated were the least safe.
Q. Thank you.
A. That's my best bet at that particular process, off-the-cuff.
Q. If we just go further down that paragraph, please, Henry, you say this:

"My decisions on product use were made on the basis of clinical need, suitability of the product for individual patient and their particular problem at the time, availability and cost."

Now, I understand each of those factors and what they mean. There's no reference there to safety.
A. Well, it would have come in to the suitability of the product of the individual patient, I think. But I take your point. I haven't actually used the word "safety" there. I accept that. But I think safety would have been an issue. The only difficulty was that, having made those comments that I made earlier, it isn't always clear what is the safest product.
Q. In terms of the factors that you have set out there --

clinical need, suitability of product for the particular patient, availability and cost -- were any of those factors, generally speaking -- did they carry more weight in your decision-making process than others, or were they all equally balanced?
A. I think the most important thing is the suitability of the product for the individual patient and their particular problem at the time. That is, the overriding question is: what is the right thing for a patient?

The issue of availability is obviously very important because if something isn't available, it's not available. I don't think cost was ever an issue in individual patients, but obviously cost cannot be ignored, as I explained in my discussion of the business-like nature of the way the NHS went after the '70s.
Q. In relation to those with mild haemophilia, to what extent was an option of no treatment an option that you would contemplate and discuss with a patient, as opposed to a treatment which involved a risk of viral transmission?
A. The answer to that, if you're talking about bleeding, is almost never because, as I've explained in my statement, mild haemophilia is not mild bleeding, and

I can't say that often enough. I spent the whole of my career explaining to my juniors, and maybe even sometimes to my patients, that mild haemophilia does not mean mild bleeding.

Let me give you a couple of examples. I have already given you one of a patient who nearly died, had a prostate operation at the age of 70 when his Factor VIII level resting was perhaps 15/20 per cent.

I can also give you an example of a university student who was under my care who had a level of Factor VIII in, take, 15/20 per cent. He fell down the stairs I think in Aberystwyth and ignored his fall. He eventually realised he had to have some treatment, took a train from Aberystwyth to London to see me, and he had the most massive haematoma in his flank which had been developing over a week or so as he was trying to ignore it.

One of the features of people with mild haemophilia, or maybe even moderate haemophilia, is that they, quite understandably, don't really know what bleeding badly from haemophilia is like and they, quite understandably, think that if they don't do anything it will get better. It is the case, I'm afraid, that for bleeding it won't get better. It will go on bleeding until something is done about it,

and that's the history of ignoring or trying to avoid treatment for people with haemophilia. It is not a good strategy.

Now, of course, if there's a question of surgery, then the issue is: how important is the surgery and what are the risks? That, clearly, is an important issue.

Q. Other than through the continuation of your policy of using mostly cryoprecipitate for young children, did your approach to treating patients change at all in the years 1977 to '83 to reflect the risk of hepatitis?

A. I don't believe that it did.

MS RICHARDS: Sir, I note the time. I am going to move on to looking at materials relating to HIV, so that might be a convenient point at which to stop.

SIR BRIAN LANGSTAFF: Yes. I think you want to break earlier for the afternoon than would otherwise have been the case. Is that still --

MS RICHARDS: Not necessarily, sir. I think, if everyone is willing to keep going, we could keep going until 4.15 to 4.30.

SIR BRIAN LANGSTAFF: Shall we take a break for 25 minutes and come back then at -- let us make it 3.35.

(3.11 pm)

(A short break)

(3.35 pm)

MS RICHARDS: Dr Colvin, I'm going to ask you now about the developing knowledge of risk in relation to HIV.

A. Yes.

Q. Your statement says you became aware of AIDS in 1982.

When did you first become aware of reports of infection, AIDS, in haemophiliacs?

A. I think when a report would appear probably in the New England Journal. I think I may have said what I knew in my statement, actually, but I can go back to my statement. But it would have been -- as soon as it would appear in a journal like the New England, which would have been quite shortly after any announcement by the reports, I would know about it.

What I wouldn't, I think, have done would have been to have read the original American report.

Q. We'll just look at that, and then we can go through it in a chronological sequence. So could we have, please, Henry, PRSE0000523, please.

This is the MMRW from the Center for Disease Control, July 16, 1982. We can see the heading, and then we just need to look at the first two lines, I think -- two sentences:

"CDC recently received reports of three cases of

PCP among patients with haemophilia A and without underlying disease. Two have died. One remains critically ill."

Would you have read and received the MMRWs?

A. No, I wouldn't have seen that report. I was actually referring to the MMWR CDC when I said I wouldn't have seen the original report.

Q. I don't think I have got a particular New England Journal article until the January, but would you expect to have become aware of that through some form or another in the weeks that followed?

A. I would have thought so.

Q. Then if we could have, please, Henry, HCDO0000556. We're in 1982 here. That report was July 1982. This is 13 September 1982.

A. Sure.

Q. It's a meeting of the UK Haemophilia Centre Directors Hepatitis Working Party. You, of course, were not a member of it, but we can see that Dr Kernoff was.

A. Yes.

Q. If we go, please, Henry, to the last page, we can see under the heading "Acquired Immune Deficiency Syndrome":

"Following discussions at the annual general meeting of Haemophilia Centre Directors ..."

I haven't checked, Dr Colvin, to see if you were there. I'll check overnight, but I think you said you generally did attend.

"... it was agreed by the working party that as the AIDS syndrome had similarities in its epidemiology to that of hepatitis B virus infection, enquiries will be made by members of the working party to ascertain the likelihood of transmission of the disease by blood or blood products."

Do you recall any communications or discussions within UKHCDO or between you and Dr Kernoff around this time about the issue?

A. No, I don't, but that doesn't mean to say it didn't happen because, you know, it's 40 years ago.

Q. We know that in December of 1982 -- again, the initial source is the MMWRs -- there was a report of what we've been referring to as the San Francisco baby case.

A. Yes, I know.

Q. Do you recall learning about that?

A. No, I don't.

Q. Then we'll come, then, January 1983, to the New England Journal of Medicine, which I think you would have seen. Henry, PRSE0002410.

We can see the date here at the top of the page,

13 January '83, New England Journal of Medicine, "AIDS and preventive treatment in haemophilia".

If we go to the second page, please, Henry, I'll just pick it up at the bottom of the page where it says this:

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

Then:

"The studies reported in this issue in vitro abnormalities of immuno-regulation but the numbers are too small for definitive comparison of the risks of different modes of treatment. Unfortunately, the data are consistent with a greater potential for AIDS in the population treated with concentrate. 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."

That's the article by Jane Desforges which you would have read?

A. I would think so, yes.

Q. Do you have any recollection of reading it at the time?

A. My main recollection is my wife's complaint that I used to read the New England Journal of Medicine in bed at this time before I went to sleep. So I think it's entirely possible and likely that I would have read this because I used to read the New England Journal of Medicine regularly, and this would be an important part. I can't really conceive that I wouldn't have read it, but I don't recall reading the actual article at all today.

Q. Then in January of 1983, we know you attended a meeting at a London Airport hotel.

The reference for that, Henry, is PRSE0002647.

So if we just look at the top of the page to start with, we can see notes of meeting with Immuno at London Airport, 24 January, and the topic is "Hepatitis-reduced Factor VII and Factor IX concentrates for haemophilia therapy".

Could we go to the last page please, Henry. We can see there the list of attendees, and we can see a few lines down it includes your name.

Now, do you have any recollection of that meeting and how it came about?

A. No, I don't.

Q. If we look further up the page, please, Henry -- if we go to the previous page, sorry, and we go to the

second half, under the heading "Acquired Immunodeficiency Syndrome", it says this:

"This was discussed in the after-lunch period. Dr Craske summarised the current position. He gave a clinical description of the AIDS syndrome."

Then we see further information in relation to that set out in the second paragraph and then, if we keep going down, please, Henry, we pick it up towards the bottom of the page:

"Up to 10 December 1982, some 800 people had been reported as suffering from the AIDS, and there was a 45 per cent mortality. Ten haemophiliacs in the US have been affected, and five have died. The youngest was aged seven. All cases have had prolonged treatment with Factor VIII, but there is no specific implication of one particular product or batch. Other cases involving blood and blood product transmission have included platelets transfused in three cases. In one of these cases, one of the donors was a young New York man in his 20s. A second case was a 20-month-old child with rhesus HDN who had received several units, including platelets known to have come from a homosexual donor who was asymptomatic at the time but who later died. The child has developed autoimmune haemolytic anaemia and a possible AIDS

state."

That's the San Francisco baby case. If we go on to the next page, please, Henry:

"The incubation period for the syndrome appears to be six months to two years. In the UK so far, only one or two cases have been reported from the communicable diseases centre. The infectious precautions include discouraging homosexuals from donating blood or organs. Protocols from the US have been considered by the Hepatitis Working Party in the UK. Apparently, the American fractionation companies are very aware of the problem and are taking some unspecified measures to screen out such donors.

The attention of the meeting was then drawn to the two articles [and we've looked at one of them, Dr Colvin] on the editorial in the New England Journal of Medicine on 13 January which, in summary, indicates that the T48 ratios among haemophiliacs receiving Factor VIII is greater among those who have been exposed to concentrates than those exposed to cryoprecipitate only. However, cryoprecipitate in the US comes from volunteer unpaid donors and therefore are presumably well motivated people. Final comments on the possible nature of the transmissible agents indicated that there may not be just one agent but

a mixture, i.e. a barrage of viruses including hepatitis B, non-A, non-B, CMV and many others, possibly transmitted from asymptomatic healthy blood donors."

Now, I've read that effectively into your evidence because, clearly, on any view, by 24 January, you would have been up-to-date with this information?

A. Yes, sure.

Q. The attention of those present was expressly being drawn to the New England Journal of Medicine editorial.

Can you recall anything about the discussion at that meeting on this issue or any other?

A. I have already explained, I don't recall the meeting at all.

Q. Would you accept, seeing this material and the New England Journal -- and I know you have been following the evidence over the last couple of weeks, but by the beginning of 1983 or, in any event, by 24 January 1983, you would have been aware that there was a risk to haemophiliacs of AIDS?

A. Yes.

Q. That the most likely route of transmission of AIDS for haemophiliacs was blood or blood products?

A. Yes.

Q. We then -- if we go to BART0000679, please. This is -- if we just zoom in slightly, Henry, thank you. This a further meeting of the North East Thames Region Association of Haematologists Working Party. It's 9 February, so it's not long after the meeting that we've just looked at. You are there. Dr Kernoff and others are there.

If we just look down over what's discussed, we see there's a discussion about self-sufficiency for Factor VIII concentrate production. If we look down towards the bottom of the page, there's an issue about cross-charging and then, the end of the page, an aim to produce all Factor VIII in the region from local screened donors.

Then if we go to the next page, we can see there's then a discussion about designation of haemophilia centres. Then -- if we go further down, please, Henry -- collection of regional statistics, domiciliary, haemophilia nursing sister.

What is conspicuous by its absence is any discussion of AIDS at that stage locally.

Are you able to say why that wasn't by now at least on the agenda, even if not high on the agenda, for this working party?

A. I'm not able to. Perhaps I could make a very brief

comment about the previous minute because one of the features of immunodeficiency in people with haemophilia was thought to be the exposure to factor concentrates of itself. Now, I never did any research in this area at all, but I was aware of those who believed, I think incorrectly, that the exposure to Factor VIII itself was immunosuppressive and might have been related to what had happened.

Now, of course, I've agreed entirely to what you asked me earlier, but I think there was a sense in which some people thought that there was an intrinsic tendency for factor concentrate to have an effect on immunity.

Q. But whether that explains the non-discussion of the issue at this meeting --

A. Only in the sense that if people believed that, they might have taken a different view to the one that we've just discussed, and in which case they wouldn't have thought it necessary to talk about this. I think that's unusual and unlikely, but you asked me to think of any reason I could possibly think of as to why this wasn't discussed, and that was the only one I could think of.

Q. But that wasn't a view to which you subscribed, and presumably at some time during the first half of 1983,

you must have had some of discussions with Dr Kernoff about AIDS?

A. That's very likely, but I can't remember the exact dates because we spoke together very often.

Q. No, I understand that, but presumably you would recall if he had come up with an unconventional theory about the link with AIDS?

A. I don't think that Peter particularly had such an unconventional link. All I'm saying is that I knew that around the country there were those who were studying the effect of concentrate on the body's immune system. That's all I'm saying.

SIR BRIAN LANGSTAFF: May I just ask, I suppose if one treats that as a possibility and one treats an infectious agent such as a virus as a possibility, the transmission on both cases would occur, on either theory, through blood products, would it not?

A. Sorry, could you explain that, sir?

SIR BRIAN LANGSTAFF: Yes.

The risk to which counsel has alerted you --

A. Yes --

SIR BRIAN LANGSTAFF: -- discussed at the meeting in January at Heathrow, which you can't remember, discussed in the New England Journal of Medicine, was a risk of blood products transferring some cause of

AIDS to those who are haemophiliac.

It doesn't much matter, for those purposes, for that analysis, whether the cause was viral or the abnormal proteins found in factor concentrate or whatever, does it?

A. Well, it would -- I mean, let's just say for a moment, which clearly is not the case, that there was something about Factor VIII concentrate which inhibited the immune system, then that of itself could be the cause of an immunodeficiency condition, in which case a virus wouldn't necessarily be involved. I agree that that's not likely but it was considered.

The other possibility is that if it was some kind of virus infection and people have been exposed to a very large amount of concentrate, it might be that those who had been very heavily exposed to concentrate might be more vulnerable to the immune deficiency illness than those who had not.

But, I mean, I'm not trying to say to counsel or you, sir, that I don't believe and didn't believe at this point there was any transmissible agent, I think there was, it's just that counsel had asked me whether I could think of any reason why it wasn't discussed at the February meeting.

SIR BRIAN LANGSTAFF: I think what I was putting to you

was: On either view, what was doing it was getting the factor concentrate?

A. Yes.

SIR BRIAN LANGSTAFF: That was all I was asking.

A. Yes, of course.

MS RICHARDS: As well as the probability that this was a condition transmissible by blood products or by blood, would you agree that by January 1983, looking at -- even if one just looks at the New England Journal and the account given at that meeting at The London airport hotel, it was always known at that stage to have a very high mortality rate.

A. Certainly the condition of AIDS was known to have a high mortality, yes, of course.

Q. It seemed also to be apparent, and is expressly referred to in the notes of the meeting in January 1983, that there may be a significant lapse of time before the symptoms present themselves?

A. Yes.

Q. So the fact that there were only a few cases at that point identified wouldn't necessarily be a reliable guide to the true extent of the risk?

A. Exactly.

Q. Can we look at the 1983 returns that you made to UKHCDO.

Henry, it should be at HCDO0000177_003. Thank you.

So we can see this sample return. These are the annuals runs for 1983 of materials used to treat haemophilia A patients, carriers of haemophilia A and von Willebrand's disease patients. Centre is The London Hospital. You are identified as the director. As I understand it from Dr Winter, this is a return that would be filled in at the beginning of the following year?

A. Yes.

Q. So the aim is to give a picture of product usage during the 1983 calendar year?

A. Indeed.

Q. If we look at the figures for haemophilia A patients, total used at hospital in-patients and out-patients, for cryoprecipitate we've got -- well, we've got two figures. One is a figure in packs. Is the other figure that's written there the figure in units?

A. It might be. I don't know who's written that figure because there's no exact figure that you can put on the number of units. But you might have expected something like 100 or just a bit less than 100 units per pack. So it's not very far off. Somebody's attempt to work out how many units it might be.

Q. So that's your not handwriting anyway?

A. I don't believe so, no.

Q. So we can see that anyway you are using cryoprecipitate to that amount.

We then have the figure, still in the column for hospital treatment, for NHS human Factor VIII concentrate, 336,645 units. Then we can see the figures -- in terms of commercial usage you're using Koate to the magnitude of 182,550 units, and Kryobulin 108,052 units. So in terms of in-patient usage, it's a mix of NHS Factor VIII and commercial Factor VIII with some cryoprecipitate?

A. Yes.

Q. Then if we look at home treatment, we can see that in 1983 there's no cryoprecipitate there identified for home treatment?

A. Of course.

Q. We can see the majority then for home treatment is NHS human Factor VIII concentrate, 763,747, but there is some Factor VIII, some Koate, some Hemofil and a slightly larger amount of Kryobulin being used for home treatment?

A. Yes.

Q. Then if we just look across, for the sake of completeness, we've got for carriers for haemophilia A

you're using DDAVP and tranexamic acid. I think that that's only one patient, we can see from the top of the page. Then for von Willebrand's disease patients, hospital provision is cryoprecipitate seems to be, in fact, the only treatment that's been used. Is that a correct reading?

A. That looks correct to me.

Q. Nine patients were treated but did not receive blood products. Do you know what that refers to?

A. It might be patients who perhaps had menstrual difficulties who were given hormone therapy. It might be somebody who came up for something else and perhaps they had a wart on their hand and was given treatment for that. I mean, it could be almost anything. But I think it implies that we knew they had been to the hospital and been consulted but didn't actually get any particular haemostatic treatment.

Q. Then if we look at --

A. Sorry, haemostatic means things to stop the bleeding.

Q. Then if we look at the top of the page, just in terms of the numbers of patients, we've got:

"Total number of haemophilia A patients treated during the year: 78.

"... carriers of haemophilia A ...: 1.

"... von Willebrand's disease patients

treated ...: 16."

Then if we go to HCDO0000177_004, please, Henry, we can see this is the annual return for 1983 of material used for the treatment of haemophilia A patients who have inhibitors.

Although the unit has been written in the cryoprecipitate column, that's been crossed out and an arrow drawn?

A. Yes.

Q. So is it a fair inference that that should have been a record of NHS Factor VIII concentrate?

A. Yes, I am sure it was, but it's a tiny amount. It's hard to know why anybody would be given that amount of NHS concentrate for an inhibitor because it wouldn't work anyway, but I mean, it's impossible to judge what that means, I think.

Q. Then towards the bottom of the page we can see "Porcine Factor VIII [the] hyate C", 11000 units.

A. At that time, if somebody had a very low titer inhibitor that was responsive to porcine Factor VIII, that's what we would have given.

What's remarkable, in a way, in this record for 1983 is that I had almost nobody with an inhibitor who was being treated.

Q. Yes. Of course this is only a snapshot because we

don't have returns I think in equivalent form for earlier years.

If we just look towards the top of that page, we can see in terms of those with inhibitors, that's reference to two patients being treated.

Then if we can just go to the return in relation to haemophilia B for the same year, HCDO0000177_005, and we can see here that you have treated 11 haemophilia B patients during the year and one carrier of haemophilia B during the year.

Then in relation to the haemophilia B patients both in hospital and for home treatment, the usage is NHS Factor IX concentrate, and then there's a small amount of fresh frozen plasma that's been used for the hospital treatment of a carrier of haemophilia B?

A. That's a rather strange entry, actually, because -- I'm quite pleased to see it because it implies that I realised that, for a carrier of haemophilia B, there was a risk of infection and that I was using fresh frozen plasma 3 bags which only contained the risk of three people's infection risk.

So I might have decided, and it wouldn't have been the best thing to do, to give a carrier, for whatever reason I don't know, a Factor IX concentrate. It was much better to give those three bags of fresh

frozen plasma, however out-of-date such an idea was.

Q. So that tells us the products that you were using simply in the calendar year of 1983. Other than the point you have just made about fresh frozen plasma, does what we have seen in those returns suggest any change of approach on your part or is that essentially consistent with how you had generally been treating patients?

A. I think it's consistent, not least because it -- I'm relatively pleased to see that it was the case that the majority of my home treatment patients were treated with NHS concentrate and that we were using some NHS concentrate in the hospital, which was appropriate, but inevitably, because of the shortfall, we were using a significant quantity of commercial concentrate in the hospital.

I can't explain the commercial concentrate in the home. It was, I think, about 10 per cent of the total usage. Of course, at this distance it's impossible for me to tell why that was the case. But it doesn't altogether surprise me.

Q. Now having understood by January 1983 that there is this risk of AIDS potentially affecting haemophiliacs with high mortality rate and so on, as far as you can recall, did you, in the course of the year that

followed, make any changes to your approach to treating patients?

A. Well, if you look at the paper that I wrote about cryoprecipitate, you will see that the patients who were treated -- in a rather unusual way -- with cryoprecipitate were treated between 1982 and 1984. So I think the implication of that is that I was thinking about the risk, and I think that I have to rely on you to tell me when you want me to talk about that paper.

Q. Let me see if I can find the reference to it, Dr Colvin.

A. I mention it now only because it shows that I was thinking about it.

Q. We have it somewhere. It may be I need to come back to that in the morning, Dr Colvin, because I can't find the reference currently. I can find a reference to a study by you on heat treatment but I know there is one in relation to usage of cryoprecipitate, so it may be we can put that on screen tomorrow morning.

What, if any, recollection do you have of any conscious rethinking of your approach to treatment in 1983?

A. I think that, again, if one thinks about the little work we did, I think it would have been to try to

minimise the risk where it was sensible and possible to do so. But it's very difficult at 40 years distance to give you a clear view from my memory.

Q. Just going through the course of 1983, we can see that in June 1983 you received a letter, as did other directors, from Professors Bloom and Dr Rizza. It's BART0000844.

We can see, Dr Colvin, this is a letter dated 24 June 1983. We've seen it in a similar form sent to others but this is the version that's actually addressed to Professor Jenkins and to you.

A. Indeed.

Q. It's headed "Acquired Immune Deficiency Syndrome". It refers to a meeting of Reference Centre Directors on 13 May 1983 to discuss the problem in haemophilia. Then in the second paragraph it says this:

"At the above mentioned meeting on May 13th, the following general recommendations were agreed.

"1. For mildly affected patients with haemophilia A order 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 many Directors."

Would that have been your usual practice, in any event, at that time?

A. Yes. Yes, it would.

I can give you the reference for the cryoprecipitate study if you would like it now. Perhaps you would rather tomorrow morning?

Q. Do you have the --

A. It's PRSE0003838.

But yes, it would have been.

Q. We will come back to the letter but I am happy to look at the study.

A. May I -- oh, sorry.

Q. So this is the study that you were referring to?

A. Yes.

Q. "A prospective study of cryoprecipitate administration: absence of evidence of virus infection."

The summary of it is:

"In a prospective study of cryoprecipitate administration to patients who had never received large pool concentrates, no evidence of hepatitis or HIV infection was detected in a follow-up period of one year. Following the introduction of screening of blood donors for anti-HIV in the UK in October 1985, the use of cryoprecipitate in selected cases should be

reconsidered."

I think you had an observation you wanted to make about --

A. Can I explain what was happening --

Q. Yes.

A. -- because I think it is really quite important.

First of all, this is not really research. What it is, is an analysis of a clinical decision that I had made on clinical grounds, and you'll see later in the paper, that I've said some patients are not suitable for DDAVP. So I had considered using DDAVP in these patients. It's very important because you might say, are you, Dr Colvin, bringing people to the risk of cryoprecipitate when they could have DDAVP which wouldn't be a method.

But the position was that -- there was one patient I think with a very severe haemarthrosis of the knee with mild haemophilia, and another few patients with von Willebrand's disease who were having elective surgery that I didn't think was appropriate for DDAVP for the reasons that I've explained.

So for these patients, I would have said to them -- this is, I think, between '82 and '84. I would have said to them, "I am concerned about the safety of the concentrates that we need to use for

your operation. My view is that for this relatively minor operation, I can use cryoprecipitate to treat you, that there is of course a risk of viral infection with cryoprecipitate, and therefore, as we go in to do this surgical procedure, I would like to have your consent to take blood samples after the operation to confirm that you haven't had an infection."

So this is not research that needs a research ethics approval; it is a study of selected clinical practice. Now, you might say, well, did you give your patients the opportunity to have DDAVP? And the answer is: no, I didn't because I didn't think it was clinically indicated. I think it's very important for you and Sir Brian to understand what this study actually means.

But by the time it was published, cryoprecipitate was dead because it's published I think in '88 or '87, and it's sent to publication in '86. So by the time it's published, it's actual history. But it shows that I was interested in '82 in trying to keep these particular patients with mild-ish von Willebrand's disease and a bad haemarthrosis using the concentrate that might be appropriate for this advice before it was given.

Q. Yes. If we go back to the letter of advice, Henry, so

it was BART0000844. We were looking at the paragraph numbered 1, if we just go down a little, Henry. Thank you. The mildly affected patients, von Willebrand's, minor lesions treatment with DDAVP. Then if we go to paragraph 2:

"For treatment of children 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."

We discussed the existing policy you had in relation to the treatment of children, Dr Colvin. In terms of patients unexposed to imported concentrates, I think your answer earlier was that, in your clinic, that would have been largely children, in any event; is that correct?

A. Sorry, say that again.

Q. Sorry. I had asked you about whether you had any particular policy for patients who had previously been untreated, and your response, I think, was that those would generally be children?

A. Probably, yes --

(Overspeaking)

Q. The category here -- you have children, we have mildly affected patients, and then patients unexposed to

imported concentrate. So that's not quite completely untreated patients but patients who haven't previously had commercial concentrates. Did you have any particular policy or practice in relation to that category of patients?

A. So this is where the word "circumspect" becomes very important and the policy was that if we were going to do major surgery on a patient at that era, then I only had the option of using commercial concentrate.

Q. Would you agree with me that this is a document that is very much leaving matters still to the judgment of the individual Haemophilia Centre Director?

A. So we, of course, heard the discussion over the last few days, including Mark Winter's discussion, about the degree to which the UK Haemophilia Centre Directors organisation, and the Reference Centre Directors in particular, gave valuable advice and I think, in retrospect, this advice could have been clearer and more prescriptive.

But it is the case that guidelines or advice is only ever guidelines and advice. From my medico-legal experience over many years, I have noticed many of the problems in medico-legal practice are because people haven't perhaps read the guidelines or, more importantly, when they have read the guidelines and

have a different view or take a view of interpretation, they don't write it in the notes. I have always been a very keen note writer, and I think my junior staff in the past got rather tired of me writing notes.

But I think it's very difficult, and I would have appreciated more advice from UKHCDO, and of course we haven't yet discussed it, but the Galbraith letter becomes very important in this context, which you may be about to show me.

Q. I may deal with that tomorrow, Dr Colvin.

But just whilst we're still looking at this, would you agree that, in the second paragraph, for children mildly affected, those who haven't previously had commercial concentrates, this isn't even saying: prioritise cryoprecipitate over factor concentrates. It's saying: prioritise NHS whatever the nature of whether it's cryoprecipitate or factor concentrates over commercial.

A. Yes, it does say that.

Q. In your evidence to the Archer Inquiry about this advice, you observed that the advice to give children and mildly affected patients NHS products meant that those who weren't children or weren't mildly affected were probably going to be treated with commercial

products. It might mean certain cohorts more likely to receive commercial products than hitherto?

A. That, of course, is about resource allocation.

Q. Did this advice have any effect upon your policy of using NHS concentrates for home treatment?

A. I don't think so, no.

Q. We can see from the return that we looked at, as a matter of fact, you did continue to use commercial concentrates not to the same extent as NHS concentrates but still to a reasonably significant degree.

A. It looks like that. Obviously, I have no memory of how or why but this is the example of the statistics.

MS RICHARDS: Sir, I note the time. I've got a number of further documents I need to explore with Dr Colvin, so it might be this is a convenient point at which to break and pick it up in the morning.

SIR BRIAN LANGSTAFF: Yes, certainly. We'll do that.

A. May I make a comment on that document?

MS RICHARDS: This one here?

A. Yes.

Q. Yes, certainly.

A. I mean, I have it in front of me. If we go to the bottom of page 1, item 2, it reads:

"Another point concerns the proposed trials of

cryoprecipitate or NHS freeze-dried concentrate. It actually says:

"Many directors already reserve supplies and it would be circumspect to continue this policy."

It could be read literally as meaning whatever the directors are currently doing, they go on doing. It doesn't say anything about recommending anything to anyone else.

A. I think it also implies, sir, that if patients on home treatment were on imported concentrates, they should remain on imported concentrates.

MS RICHARDS: Do you recall -- I know I should finish but, picking up on that point, do you recall whether that was the position for your patients?

A. I don't.

Q. Thank you.

SIR BRIAN LANGSTAFF: The language is just a bit -- if I say "mealy-mouthed" it may be misunderstood, but it's not very clear.

A. I certainly think it was less than helpful now that I think back 40 years.

SIR BRIAN LANGSTAFF: Yes, thank you very much. Tomorrow morning, 10 o'clock in that case.

(4.16 pm)

(Adjourned until 10.00 am the following day)

hepatitis-reduced factor concentrates. There is no evidence that the processes involved in the manufacture of these inactivate any other hypothetical viruses" and then it goes on over the page.

"It is still important that the effectiveness of imported hepatitis-reduced concentrate vis-a-vis hepatitis is subjected to formal clinical trials in mild haemophiliacs notwithstanding our general recommendation above. Directors are urged not [underlined] to use these concentrates randomly on a named patient basis."

That may become important if you were to want to discuss with me Dr Winter's evidence from his policies in 1984.

MS RICHARDS: Okay, thank you.

SIR BRIAN LANGSTAFF: Yes, the only other thing, perhaps, if we can just go back to the first page of that letter -- can we go back to the previous page please, Henry -- and look at the recommendation number 2, there may be a mismatch between what it says literally and how it was meant to be understood.

You have understood it, as I think it may well have been meant to be understood, that the guidance is for those who are mildly affected or previously unexposed to imported concentrates should have

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