Friday, 17 June 2011

(9.30 am)

THE CHAIRMAN: Good morning.

PROFESSOR CHRISTOPHER LUDLAM (continued)

Questions by MR GARDINER (continued)

MR GARDINER: Professor Ludlam, you are appearing at the Inquiry, I think, for the third time, a third session.

A. That's correct.

Q. Thank you. You appeared previously on 30 March to talk about statistics and you appeared on 3 and 4 May to talk about the B2 topic?

A. That's correct.

Q. You have provided the Inquiry with several statements about the topic that we are looking at today. I think it's helpful just to remind ourselves what that topic is. So could we have on the screen, please, topic B5? We see on the right-hand side of the page the topic that we are looking at in this session is B5A:

"The information given to patients (or their parents) about the risk of AIDS before their treatment with blood or blood products.

"B5B) The tracing and testing of patients who might have been exposed to the virus through their treatment with blood or blood products.

"B5C) The information given to patients who might

have been infected or who were found to be infected and their families.

"B5D) And in particular the circumstances in which those patients known collectively as the Edinburgh cohort became infected with HIV, the testing of such patients for HIV and the information given to them about their infection."

There are two statements I particularly want to focus on, which you have given the Inquiry. The first one is [PEN0120351]. This has a heading "Long-term safety monitoring for transfusion-transmitted infections". I think that you should have a paper copy of that, Professor Ludlam. Thank you.

The other document that I would like to look at in connection with this topic is [PEN0120774]. These are the notes of a meeting between yourself and Gemma Lovell, an Inquiry team member, in which B5 issues were discussed. That's right, isn't it?

A. That is correct, yes.

Q. It's fair to say, Professor Ludlam, that these notes went through several revisions by yourself in order to arrive at what you thought was a correct answer to the questions that you were being given. Is that right?

A. That's correct, and also additional questions were posed when I received the draft.

Q. Yes. Thank you.

I would like to approach this topic chronologically and in order to do so, we need to move between these two documents. But just to get a context, I think I'm right in saying that you started at the Edinburgh haemophilia centre at the beginning of 1980?

A. That's correct, yes.

Q. Could you just remind us how many haemophilia patients you had under your care at the beginning of 1980?

A. Approximately 170.

Q. Which other doctors and nurses were there at the centre who helped you to treat these patients?

A. I was the only consultant. There were two consultants in the Royal Infirmary, who had to cover all the haematology service, so not all my time was devoted to haemophilia. I looked after lots of patients with leukaemia, lymphomas, provided consultation about patients in other wards. Our catchment area in those days for general haematology was much greater. We took patients from the Borders who came up with malignant disease. So more than half my time would be spent doing things other than haemophilia.

Q. Yes. The haemophilia aspect of the care that you are providing, what other doctors and nurses were there at that time that were helping you?

A. The only assistance I had was from a registrar, a doctor in training, and a clinical lecturer, who was providing part clinical -- had part clinical duties and partly doing research.

Q. Yes.

A. We didn't have a haemophilia nurse at that stage. So it was myself really and a registrar who, like me, had many other responsibilities.

Q. Yes. Do you remember the name of the registrar?

A. Well, there were a series of registrars, but the ones that took a greater interest were Dr Robert Carr and Dr John Tucker.

Q. How long would these registrars stay with you?

A. Somewhere between two and four years.

Q. Thank you. I think you give some of the history of the centre in the long-term safety monitoring statement, so if we could have a look at that, which we have on the screen.

We see at paragraph 2 you explain:

"Historically the treatment of bleeding in haemophilia has been associated with adverse events. These include allergic reactions, haemolytic anaemia, antibodies to the deficient clotting factors ..."

And so on. Paragraph 3 you say:

"The Edinburgh Haemophilia Centre has a long

tradition, starting in the 1960s and 1970s, of systematically studying the bleeding pattern in those with haemophilia, describing arrangements at a Haemophilia Reference Centre and was amongst the first to assess hepatitis and the risks of virus transmission with the initial studies on Hepatitis B virus infection."

Then if we go down to the bottom of that page at paragraph 6 you explain what treatment was given at the centre. You say that:

"To monitor treatment-related adverse events (including infections) at clinic visits, blood would be taken for a full blood count (haemoglobin, white cell count, including enumeration of the different types of white cells and platelet count) and assessment of blood chemistry ..."

Could you just explain to us what the purpose of taking blood for a full blood count was?

A. Yes. It was important to make sure that the patient's haemoglobin and white count and platelets were in the normal range. As you saw earlier in the page, one of the complications, particularly of the early Factor VIII concentrates, was they contained antibodies to red cells and so you could get destruction of the red cells and hence anemia.

The other reason for checking the haemoglobin was that sometimes patients had silent bleeding into their gastrointestinal tract. That was not uncommon. So this was a way of being alerted to that possibility.

Q. Yes. Just reading on in that paragraph, you explain that:

"These latter samples were stored long-term in haematology and virology, as was customary for virology blood samples."

When you say "stored long-term in haematology and virology", are these two separate departments in the hospital?

A. Yes.

Q. Thank you. Over the page you say that this was considered good clinical and laboratory practice. Just to clarify that paragraph, we asked you at question 5 of the notes documents about blood that was taken and you explain that:

"Blood was regularly taken from patients when they attended the clinic for review. It was part of the routine of coming to the clinic that blood as taken. Blood was not taken every time the patient attended but was done when tests were deemed necessary. The frequency of a patient's attendances depended on their clinical situation."

Could you explain what the different clinical situations were and how they could affect how often patients would be seen in the centre?

A. At this time in the early 1980s, the patients were mostly on hospital treatment. So they were coming up quite frequently, particularly if they had severe haemophilia, to get their treatment with cryoprecipitate. So patients with severe haemophilia might come to the treatment room two or three times in a week and we would obviously see them, review them and treat them with cryoprecipitate.

If we hadn't seen them for a little while or if there was something unusual about their clinical state, then we would take these blood samples to investigate why they might not be well.

Those samples would be taken when the needle was inserted to treat them; in other words, we didn't take blood from them, put it into the tubes and come back a little while later with their treatment and puncture them again. We tried to do it all at the same time.

There would be other patients who were perhaps on home treatment and who we might see every three or four months if there weren't problems. We were keen to see them reasonably regularly to make sure that they didn't have any chronic bleeds that weren't being adequately

treated, because you will recall, this is a time when we felt there was quite a shortage of Factor VIII available for patients.

Q. When you say "home treatment", are you talking about with cryoprecipitate or with concentrate?

A. With concentrates.

Q. With concentrates?

A. Yes.

Q. Thank you.

A. Those patients would come up for review every three or four months and part of the regular review was to check the -- those blood tests that I itemised earlier: the haemoglobin, the chemistry and potentially the virology.

Q. Yes. Who would the patients be seen by on those occasions?

A. For the reviews, coming to a clinic appointment, almost exclusively me, sometimes my registrar. When they presented with an acute bleed, it would either be myself or my registrar, just depending who was free.

Q. Thank you. Under the heading of "Information about the risk of infection", we asked you a question about this early period. Could we go to question 1 of the notes, which is 0774. The question was:

"In the early 1980s when you were working as a consultant in Edinburgh, did you discuss the risk of

using factor concentrates (for example, infection with Hepatitis B and, subsequently, NANB hepatitis) with your patients?"

You answered that:

"It was well-known amongst patients in the early 1980s that there was a risk of hepatitis from treatment with factor concentrates including cryoprecipitate. Patients on home treatment signed consent forms in which infection was specifically mentioned ..."

You say:

"In the 1970s and 1980s there was literature available from the Haemophilia Society."

But I think the answer to the question was you did discuss the risk of hepatitis with many of your patients because they were at risk and had hepatitis and some became jaundiced. Could you explain how you did that?

A. In a number of ways. Clearly, one extreme, if the patient became jaundiced, then one had to discuss that with them and explain how it would have arisen but it was well-known that the blood tests we were doing, including measuring liver function tests -- and these would often be discussed with patients when they came back subsequently to review appointments. Patients were generous enough, for example, to make themselves available for teaching students, and we had patients in

the hospital quite frequently in those days because of inadequate treatment, and they were generous enough to allow me to bring medical students, for example, to come and see them and we would have quite a full discussion about the risks of treatment.

So there was a whole range of times when patients would get to learn about hepatitis in general. If they weren't feeling ill, came up one day and were just off colour and feeling a bit sick, one would then begin to wonder whether they had got a dose of hepatitis. So it was very common knowledge that this was a risk and the patients knew that I had an interest in monitoring it; hence these blood samples in virology and the copies in haematology.

THE CHAIRMAN: Professor, I wonder if I could go back a little in time because Mr Gardiner's questions so far, quite understandably, take up your approach in the early 1980s but would I be right in understanding that you effectively inherited a cohort of patients who had already had considerable experience of treatment in the hospital?

A. Yes, I inherited patients who had been looked after, I would say extremely well and obsessionally by my predecessor, Dr Howard Davies, and he was very open with the patients about their situations and he, as I think

I may have emphasised when I was here before, was very keen to try and avoid the use of commercial concentrates, mostly because the blood came from North America. And there was a lot of discussion at that time as to how many different sorts of hepatitis viruses there might be and he felt that it was better for patients, if you like, if they are going to get hepatitis, to get it, if I can put it this way -- the local type of hepatitis because some of them may have immunity to it anyway having been acquired through the community, as happens, for example, with Hepatitis A.

THE CHAIRMAN: I think I can see an aspect of that. What I was concerned with at the moment was whether it would be right or wrong to get the impression that you were introducing patients to knowledge of hepatitis risks when the alternative explanation might be that they came to you well equipped with a body of knowledge.

A. They came with me. They were very well-informed.

MR GARDINER: It seems to me that you are describing information passing to patients incidentally as opposed to being passed to them deliberately by you. Is that fair?

A. I think a lot of information-giving to people with chronic disorders, who you are seeing very frequently, is done in a sense on a need to know basis and as it

arises in their clinical care. There were also meetings, particularly of the local Haemophilia Society, the patients' group who met, and we were invited to go along and talk to them about new developments and our activities and the way we saw haemophilia services being provisioned.

Q. As far as preferring SNBTS concentrates as opposed to commercial concentrates, is that something that you discussed with your patients? Did you explain to them why this was the type of concentrate that you were favouring?

A. Yes, in a number of ways. First of all, it was, if you like, the standard treatment. That's what was on offer.

Q. Yes.

A. But that was because we thought it was safer than commercial concentrates. That -- because I was so keen for my patients, if I can put it that way, the Edinburgh patients, not to be exposed to commercial concentrates, if possible, I gave each of them a little slip of paper to put in their haemophilia card -- this is the card that they all carry --

Q. Yes.

A. -- to say that "This patient had only been treated" or predominantly treated "with NHS concentrate", and if they went to another haemophilia centre down in England,

if they were travelling -- asked them to produce their haemophilia card -- with a slip of paper in signed by me saying:

"If possible, please treat with cryoprecipitate or NHS concentrate. But obviously, if you don't have that, then commercial concentrate has to be used."

Q. Yes, I think you told us about that the last time you were here, Professor Ludlam. Did you explain to your patients why you were asking them to carry this piece of paper?

A. Well, yes, because if they went to another haemophilia centre, it was additional evidence as to how I should like them treated because they, in a sense, were registered with my centre.

Q. Yes.

A. And they might go down to Manchester or Bournemouth or London, you know, on holiday or for a trip, and once you have been exposed to commercial concentrate -- and, as we have seen subsequently -- studied subsequently -- they all contained hepatitis virus -- there was no going back.

Q. I follow that. I'm really focusing on communications from doctor to patient and I'm asking you if you explained to your patients why this was that you were following this practice in giving them the bit of paper

to give to other centres?

A. Oh, yes, that's self-evident. Yes, yes, I did, yes.

Q. It was self-evident to them or you explained it to them?

A. Well, I would give them the piece of paper and I would say, "This is why we are doing it".

Q. In your written answer you mentioned a consent form and could we have a look at [PEN0120853]? Is that an example of a consent form?

A. It is, devised by my predecessor.

Q. Yes, thank you. Just reading from the bottom five lines, where it says:

"I have had explained to me in detail the possible risk of self-medication with this material, including the risk of an allergic reaction to it and of the problems associated with any transfusion, such as the risk of introducing infection or air into my vein, and I am willing to accept these risks."

Professor Ludlam, that last passage there, the risk of introducing infection, is that not a risk of introducing infection from the skin in the process of performing the injection, as opposed to an infection that's actually coming from the concentrate?

A. It is possible to introduce infection from the skin. It's probably an overrated risk but there is certainly a risk. If you put a needle through skin that has got

bacteria in, it can be pushed into the vein and cause infection. But this, I think, clearly relates to the factor concentrate because it says "or air into my vein", and that is if there is air in the syringe. So this refers to what is being introduced into the vein from the syringe.

Q. Yes.

A. Sometimes, when you draw up the clotting factor into the syringe, you get some air in the syringe and it's important to expel that before you infuse it because if you infuse a lot of air into the circulation, the circulation gets impeded.

Q. Yes. So you think, when the form says "the risk of introducing infection", that is really referring to the risk of introducing viruses?

A. Yes, or bacteria.

Q. Yes. It's not completely clear, is it?

A. Well, in a sense it covers viruses and bacteria and fungi. And they have been bottles of Factor VIII in which there has been manufacturing failure, in which there has been fungus. Those have never reached distribution but, you know, it was -- in those days it was an open system for manufacturing concentrates. It wasn't closed.

Q. Yes. I think in any event you are in no doubt that at

that time your patients had no doubt that there was a risk of infection from viruses. Is that right?

A. That is correct.

Q. Yes. Can we move on to the next question, which is also under the topic of the risk of infection. This is in the notes. The question is:

"When the possibility that AIDS was a blood-borne disease which affected haemophiliacs became apparent ..."

The question, it is put:

" ... (around December 1982) did you discuss the implications with your patients before continuing to use factor concentrate therapy?"

And you say:

"At that time, most of my patients were being treated with NHS concentrates produced in Scotland. In December 1982 there was no evidence of AIDS in Scotland and we therefore perceived the risk or infection from NHS factor concentrates ..."

Over the page now:

"... (which were manufactured from blood collected in Scotland) to be small."

Just pausing there, when you say "we" who are you referring to by "we" there?

A. Myself and the registrar who would be working with me.

Q. So the doctors?
A. The doctors. I think by that stage we were fortunate enough to have our first very able haemophilia sister.
Q. Yes. So just reading on there, you say:
"I did not discuss AIDS with my patients at this time unless they specifically asked about it."
You say:
"I do not recall there being much concern."
Can I ask you, professor, why did you not discuss AIDS with your patients in December 1982?
A. I think this may not be entirely accurate. It is very difficult, in the continuum of looking after patients over 30 years, to remember exactly what happened when.
But I was interested that in one of the patient witness statements, of the patients who came here, the patient made spontaneous -- spontaneously put into the statement that I had discussed AIDS with him and his mother at a clinic visit. So I think we clearly were discussing it with patients --
Q. If that witness' recollection is correct?
A. If that witness' recollection -- I'm gathering what evidence there is.
Q. Yes.
A. If patients had asked about AIDS -- and I should say by this stage, December 1982, there were seven patients in

the United States with haemophilia with AIDS, and I know at my last appearance here there was much discussion about when it became -- ought to have been considered to be clear that AIDS was due to a virus. And the case that was discussed, the child that got AIDS, possibly from a platelet transfusion, was thought of as a tipping point.

Q. Yes. What period is that?

A. That's December 1982. And I think I would like to put my perspective, which was that it was a gradually emerging picture during early 1983 that it was -- the agent, whatever it was, was probably transmitted by clotting factor concentrates. So it wasn't a sudden acceptance, either by me or by the community. And there is lots of evidence, some of which I think you have heard already, from people more expert in this than me.

Q. Yes.

A. It was -- if I was to discuss it with patients, I wouldn't have a great deal to say to them in a sense because one could say, "Well, it might be transmitted by blood products" but that would be all.

Q. Yes. I mean, at the moment we are talking about December 1982.

A. Yes.

Q. What we have in the notes here is that you did not

discuss AIDS with your patients at that time. But are you coming away from that now and -- I would like to try, Professor Ludlam, please -- I know it's difficult because it is a long time ago, but could you speak from your own recollection?

A. Well, I think -- there must have been in early 1983 -- it was becoming more evident that possibly there was a transmissible agent. At that stage I think -- I certainly wouldn't have kept it from patients. I had a very open way with discussing these things with patients.

We started doing immune tests in around the beginning of 1983, when, you know, we were beginning to get concerned on a global sense about it, and I started doing immune tests. And to make sure that they were correctly carried out in the laboratory, I labelled the blood forms "AIDS study". These would be forms that would be handed to the patients to get their blood taken and, you know, patients could read it. So I must have explained something about AIDS because I wouldn't write "AIDS study" on a form, which I then either handed to the patient or was sitting in front of the patient while they were having their blood taken, without some explanation.

Q. Yes. What you are describing there, Professor Ludlam,

seems to be information that a patient might pick up incidentally, if you like, and I'm trying to focus on your deliberate attempts to communicate a message to your patients about this risk. At the moment I'm focusing on December 1982 and are you saying to us that really the onus at that stage would be on the patient to raise the topic with you?

A. There was very little known about AIDS in haemophilia in December 1982.

Q. Yes.

A. The first three cases were reported in July in MMWR and there was a lot of uncertainty about what these might represent. By December that year, out of a population of 20,000 people with haemophilia in the United States, four more, I think, it is reported by MMWR -- by December -- so there were seven patients...

Q. What conclusion could you draw from that information at that stage? Would you be saying that there is a possibility that blood products could transmit this new virus?

A. Oh, certainly, yes.

Q. Yes.

A. Yes, that was evident on 6 July 1982 when the -- I think it was 6 or 13 July, when the MMWR report came out. That was the obvious message.

Q. I'm just looking at when that possibility would become more certain, if you like, as time went on. I think you said it was an emerging picture. When would it change?
A. I think it changed in the spring of 1983, the following year.
Q. At that stage -- it has been a possibility -- how would you describe it in the spring of 1983?
A. I think it was becoming clearer that there was some strange things happening to the immune system of people with haemophilia. A number of reports in the medical press of immune abnormalities in patients with haemophilia who were otherwise feeling well. It was -- the interpretation that you could put upon those was puzzling us. I would say that similar abnormalities were shown in gay men who were otherwise feeling well. And the question is in fact: were all these patients or all these individuals in the United States actually already infected with a latent, if you like, AIDS virus?
Q. I want to come on to that, but by spring 1983 were you routinely discussing with your patients this emerging risk of transmission of this new virus by the blood products that they were using?
A. The patients who would come up -- and certainly we would be doing -- asking if we could do the immune testing, which wasn't an extra blood sample, it was just using

the sample already collected. But as I have indicated, we had to go to the trouble of writing on the form something extra. I'm sure I would have explained to those people that there was a possibility that this new -- very new condition, called "AIDS", that we didn't really understand, might be spread by blood products.

Q. Yes.

A. Yes.

Q. So your best recollection is that those patients would have been informed of this possible risk?

A. I think I would have tempered that by saying that, "As you know, you have received only Scottish" -- or the majority of people -- "Scottish prepared Factor VIII", and at that time there were no cases of AIDS in Scotland.

Over that period, 1983, I actually made quite extensive enquiries amongst my colleagues whom I thought might see patients with AIDS and the people who might collect statistics on AIDS, and I couldn't find anyone who had any experience or knowledge of having seen someone that they thought might be someone with AIDS, or what we call "pre-AIDS" or "AIDS-related complex".

In those days there was much less intercontinental air travel and movement of people, and the population in Scotland was much more static than in North America and

even in England, and the big metropolises in England, like London and Manchester, there was a lot of coming and going of people from all parts of the world and from Africa as well.

So I don't say Scotland was isolated but, you know, we had a very stable, certainly, population of people with haemophilia, but also I think the general population was stable. For those reasons I thought the risks were small.

Q. Is that what you told these patients?

A. Yes.

Q. And --

THE CHAIRMAN: Professor, I have a concern with the use of the expression "AIDS" in the very early 1980s, stemming in part from your own use of the expression "Acquired Immune Deficiency Syndrome" as relating to biochemical change rather than an infectious agent. When would you have become, on balance, convinced that there was an HIV/AIDS, an Acquired Immune Deficiency Syndrome specifically related to a transmissible agent like a virus?

A. I think in the spring of 1983.

THE CHAIRMAN: Does that provide, as it were, a change of emphasis in your own mind as to how one would approach this syndrome? Because it seems to me that a general

question about communication about AIDS must be different. You are the communicator and what you are saying or not saying must differ at the point at which you yourself take on board the broader evidence that points to a transmissible agent. Is that an accurate comment to make?

A. No, I think that's fair.

THE CHAIRMAN: I think, Mr Gardiner, it is important that we don't confuse the overall body of evidence by talking about HIV/AIDS and your communication about it before you yourself have formed a view on that matter?

A. I appreciate -- I think it is a very important distinction, thank you.

MR GARDINER: Thank you, sir.

So, professor, did your practice change in the information that you gave your patients after spring 1983?

A. Not, I think, materially. In June 1983 there was a meeting of UK haemophilia directors from the reference centres to consider the situation that was emerging and that meeting made recommendations about treatment. We were already conforming to those recommendations and so there didn't seem to me to be a need to change my suggestions for therapy.

Q. Yes. Thank you.

THE CHAIRMAN: I think I can see that but I have to say, I am interested in the pattern of communication between you and your patients once it had become accepted by you that the probability was -- not a mathematical certainty, I know -- but the probability was that there was an HIV/AIDS condition, as we now would call it, that was caused by a transmissible agent. So I think that is important to answer Mr Gardiner's question, Professor Ludlam, in a sort of direct way, if you can.

A. Yes. What I would say to the patients is, "We think it is -- there is a blood-borne agent but I think the risk of it being in our blood supply is very small but a possibility -- but a pretty small possibility."

Q. Yes. Do we take it that that is not a discussion that you would have initiated; it would be questions that you would be responding to from your patients?

A. I think it would be part of the dialogue. We were, as reported, undertaking these immune tests and I would have explained, you know, why we were doing that and so, as part of that explanation, I would have said from my perspective, "I think it's very unlikely that whatever the agent is, is in the blood supply of Scotland", for reasons that we have rehearsed.

Q. Yes. Thank you.

When you had these discussions with your patients,

Professor Ludlam, was there any discussions about the different kinds of treatment that they could be having in the context of the emerging risk?

A. Well, the two options were cryoprecipitate or NHS concentrate, and patients were very, very keen to get on to the concentrates and -- very keen indeed -- and I was having, as I have perhaps explained when I was here before -- having to delay patients getting home treatment, they weren't very happy about that.

So I could have -- I might have mentioned that we could go back to cryoprecipitate, it wouldn't abolish the risk. It might or might not reduce it. It depends on the prevalence of the agent in the donor pool.

But I think I would say I wasn't encouraging patients to go back to cryoprecipitate if they were on concentrate and on home treatment.

Q. Yes. So do we take it that you wouldn't raise that topic yourself with your patients?

A. Probably not, but it would depend a bit on the circumstances.

Q. Yes. Could you elaborate what difference would the circumstances make?

A. Well, if there was a small child who had not had much treatment, they would probably be getting cryoprecipitate anyway because they would be being

treated in hospital. And that's the treatment we used in hospital because we kept the concentrate for home treatment. So if you like, the people that would -- preferentially one would want to convert over to cryo were probably already getting cryoprecipitate.

Q. Yes.

A. So -- and that would be in keeping with the guidelines that emerged in June 1983.

Q. Yes. So that would be following the guidelines at the meeting that you referred us to in June 1983? Thank you.

Could we have a look at question 3, which I think we still have on the screen, which really deals with the question that we have just been discussing there, which is:

"Did you consider switching your patients back to cryoprecipitate ..."

You say:

"We did consider switching patients back ... in around 1982/83 but the logistics of doing so were huge. In the late 1970s and early 1980s, Scotland and Edinburgh in particular had been highly dependent on cryoprecipitate. A large effort had gone into scaling back cryoprecipitate production and scaling up the manufacture of factor concentrate, which enabled

patients to be treated at home. Concentrate was initially in desperately short supply. We did consider whether concentrate manufacture could be reversed but this seemed such a retrograde step."

I think you are acknowledging there that it would have been possible, however, to do it?

A. It would have been possible. It would have taken time because extra equipment would have needed to be bought by the blood transfusion.

Q. Yes.

A. And the blood transfusion was putting all its effort into improving its plant for making concentrate.

Q. You go on to say:

"Switching patients back to cryoprecipitate would have required huge changes to the manufacturing practices and would have taken some time to accomplish."

I wonder if that's a little bit overstated, Professor Ludlam, but our understanding is that concentrates are, if you like, made from the cryoprecipitate. So it would be a question of stopping the production, as opposed to carrying on with more production. So is that not a bit overstated, "huge changes to the manufacturing practices"?

A. You would need to -- I daresay you have asked the Blood Transfusion Service about this, but to make

cryoprecipitate, you take the plasma in the plastic bag that has been squeezed off -- and I'm sure the Blood Transfusion has explained how they squeeze off the plasma -- into a polythene bag, snap freeze it very quickly and then if you want to make cryoprecipitate, you then allow it to melt in a fridge, then centrifuge it again and squeeze off the plasma.

It's done on a sort of one-off basis. My understanding -- my recollection is that if you are going to use the plasma for fractionation, then you take the frozen plasma and pool it into a large vat and then start the manufacturing process. So in one you are pooling a lot of plasma, the other, in a sense, each pack of cryoprecipitate is hand crafted and that takes centrifuges and personnel.

Q. Yes.

A. Is my recollection.

Q. Yes. So you are sticking to what you have said here, that it would have required huge changes, as far as --

A. We discussed it and my colleagues didn't look at all favourably upon it being able -- as being able to achieve it in the sort of timescale that you might be thinking of.

Q. Yes. Do you remember who discussed that topic and when that was?

A. I think it was through sort of informal discussions between myself probably Brian McClelland and Frank Boulton. We had offices fairly close together and used to talk about these sort of things. It may have been discussed in a rather more formal context. I can't remember.

Q. Yes. Okay. Thank you.

Just reading on in that paragraph and the context, of course, is reverting to cryoprecipitate, at the bottom of the page:

"We were also aware that doctors in the USA had attempted to move patients back to cryoprecipitate when the risk of AIDS became apparent. This move was unacceptable to the USA patients who wished to continue taking factor concentrates even though there were many people with AIDS in the USA."

I think you are referring there to Oscar Ratnoff. Is that right?

A. He was one of the principal people, yes.

Q. Although it's not in our database, I think that Oscar Ratnoff wrote a letter about this, which was published the Annals of Internal Medicine in March 1985. I think you were kind enough to give us a copy of this, Professor Ludlam. We are talking about 1983 here, and surely you wouldn't have known at that stage what

Oscar Ratnoff's experience had been with his patients in 1983. The letter is not published until 1985.

A. No, I accept that.

Q. Yes.

A. But I think what I would say is that there was no effective move in North America to using cryoprecipitate.

Q. Yes.

A. There were some centres that used a lot of -- had historically used a lot of cryoprecipitate, for example Seattle and the region around the Puget Sound -- the centre around Seattle, but despite the high -- if I can put it this way -- prevalence of AIDS in the North American population, people with haemophilia were not moving back to cryoprecipitate, although it had been suggested. And even if they had, the experience in Seattle was that there were very significant rates of HIV infection when the test became available.

So merely by moving to cryoprecipitate, you weren't going to abolish the risk of HIV; it might or might not reduce it.

Q. Yes. But that's knowledge that you gained subsequently, not in 1983.

A. Well, in 1983 I knew that patients weren't switching back to cryoprecipitate in North America.

Q. Yes. The narrow point I'm making here, Professor Ludlam, is that what Oscar Ratnoff was doing in America could not have been a factor in your thinking at that time?

A. That's probably true but I was at scientific meetings and he was someone who was always happy to let people know what his opinions were.

Q. Yes.

A. But I think for the purposes of this discussion, I would agree that this refers to the 1985 --

Q. Yes, thank you.

If we go over the page, still the context is switching to cryoprecipitate. It's what you have told us: you don't recall discussing the option of switching back to cryoprecipitate with your patients.

I would like to move on to another topic. You have mentioned it had a couple of times this morning, and this is your research into immune function in patients with haemophilia. You started a collaboration with Dr Steel at the Western General Hospital in Edinburgh in 1983. You set that out in the long-term document at 0352. So just to remind ourselves of the context here, paragraph 7:

"AIDS was first reported in three patients with haemophilia in the US in 1982. Up to this time the

cause of AIDS was not known but it had only been reported in homosexual men. In those with clinical AIDS, immune tests revealed a severe deficiency of T helper (CD4) and an increase in T suppressor, CD8 lymphocytes. In addition, many homosexual men who had no symptoms suggestive of AIDS were also found to have similar immune abnormalities, although in a milder form."

There were a number of differing explanations for that. That included:

"The possibility of a virus which may have infected a large number of such men ..."

Paragraph 8:

"In light of the observation that many asymptomatic homosexual men had immune abnormalities, studies to assess the immune status of apparently well asymptomatic haemophiliacs were immediately undertaken in the US. These demonstrated that there was a similar situation in those with haemophilia, in that many asymptomatic individuals had similar immune abnormalities to homosexual men. Again, the cause of these was unclear ..."

You say at paragraph 9:

"The finding in 1982/3 of immune abnormalities in asymptomatic apparently well individuals with

haemophilia in the US was perplexing and worrying. The cause of the immune changes was unknown and might have been related to the widespread prevalence of an AIDS virus or be due to some other side effect of Factor VIII treatment or it might even have been a previously undescribed feature of the condition of haemophilia."

In paragraph 10 you start to describe the project that you started with Dr Steel. Those three paragraphs beforehand really set the context of why you were embarking on these studies. Is that right?

A. That's correct, yes.

Q. So you say at paragraph 10:

"With the possibility that people with haemophilia had apparent immune dysfunction, which might have been related to their treatment, might be progressive and might lead to AIDS, I sought the help of a colleague, Dr (now Professor) Steel, at the Medical Research Council unit at the Western General Hospital in Edinburgh."

Could you just tell us what Professor Steel's main work was at that time at the Western General?

A. I think he would describe himself as a cell biologist. He was interested in -- or had been -- in infectious diseases and in genetics and immunology. So he seemed an appropriate person to approach and see if he could

help with this monitoring.

Q. Yes. Thank you. Just reading on in paragraph 10:

"He generously established in his laboratory the facility to measure the proportion of CD4 and CD8 lymphocytes by microscopy in patients' blood. Similar studies were set up elsewhere in the UK, including haemophilia centres in Glasgow, the Royal Free Hospital and Birmingham ..."

Reading on, paragraph 11:

"When patients attended the Edinburgh haemophilia clinic for review, blood was taken for the investigations set out in paragraph 6 ..."

Those are the ones that you have described this morning, is that right?

A. Yes.

Q. "... and sent to the haematology laboratory in the Royal Infirmary. The full blood count was assessed in the usual way, except that instead of counting 100 white cells under the microscope to quantify the number of the different types, 200 were enumerated to obtain a more accurate estimate of the number of lymphocytes, as they only form a relatively small proportion (approximately 15 to 25 per cent) ..."

Professor Ludlam, could you just take a moment and try to expand a bit on what you have mentioned there,

that rather technical description of the testing?

A. When the blood is assessed in a routine -- for routine haematology investigations, in those days it was much less automated than it is now and the sample would have its haemoglobin measured with electronic instruments. A blood film would be prepared, and that's a drop of blood on a microscope slide, and smear it out so that all the cells are singly.

It's then stained and someone looks down the -- one of our staff, laboratory staff, looks down a microscope and counts the numbers of different types of cells: the lymphocytes, which look different from polymorphs, which look different from eosinophils. There are about four or five different types and they count manually -- they have little counters for doing it -- very quick and highly skilled at it -- they count normally 100 cells so that you can then know the percentage of each of the cells.

The total number of cells is estimated through another electronic instrument. And the reason that we needed to count 200 cells was because the lymphocytes, as you see, only constitute a relatively small population, 20 per cent or so, and if you count a larger number of total white cells, you are more likely to get a precise estimate of the number of the lymphocytes.

That's important because we then divide the lymphocytes into the CD4 and the CD8 cells. So we are further subdividing the numbers. So it's very important to try and get as precise an estimate of the lymphocyte count as possible.

Q. Yes. Why was it that Dr Steel's department had that facility to perform that exercise? What expertise did they have that the other department didn't have?

A. The counting of the cells was done in our routine haematology department in the Royal Infirmary.

Q. Yes.

A. Our staff were very skilled at doing that. The samples were then couriered over to the other laboratory at the Western General Hospital, where completely different techniques were used. The blood films would be made on a glass slide and then antibodies would be put on the slide that reacted either with the CD4 cells or the CD8 cells. And then the cells that had taken up those antibodies were visualised and counted down a microscope. So there was more manual counting, initially down a microscope and, because of the small numbers, there was -- it was difficult to get really precise estimates.

Subsequently, this became automated, what are called FACS scanners became available and they counted many

more cells and you got a much better estimate. But this was very early days and this was all that was available.

Q. Yes. So the normal investigation, if you like, in the haematology department would be simply visualising the cells, whereas in Dr Steel's department, you were actually introducing an antibody and then visualising. So the sample is being changed in some way?

A. It is being further processed in a fairly precise and sophisticated way.

Q. Yes, thank you. Just sticking on paragraph 11 and reading on there:

"These samples ..."

These are the ones that are going to Dr Steel:

"... were labelled 'AIDS study' to identify them for different processing in the laboratory and they were then couriered to Dr Steel's laboratory at the Western General Hospital, where the proportion of CD4 and CD8 lymphocytes were measured. By this means, it was possible to assess the proportion of each type of lymphocyte as well as their absolute number in the blood."

That's what you have just explained to us. I think we get more details about these references if we go to the notes document at question 4. That's 0776. The question is:

"When did you start to collaborate with Dr Steel ... what records were retained and are records still available?"

You say:

"I began to collaborate with Dr Steel in early 1983 (around January/February)."

Is that from your personal recollection, Professor Ludlam?

A. Yes, I think it took us a few weeks to negotiate what we wanted to do. And so I think the first blood samples probably were sent over in about March.

Q. Yes. You say:

"The results of the lymphocyte tests carried out ... were initially recorded in paper records."

The next paragraph:

"Some of the request forms which accompanied the blood samples to haematology were added to individual patient's case notes retrospectively."

Before we look at the request forms, could you just explain to us why the request forms were added to the case notes retrospectively?

A. Well, when the request forms -- the request forms were also the report forms and they were returned to the haemophilia centre with the -- some of the results on, the results of the 200 cell count. We then entered that

and other information off the forms into the computer, along with the data that came from the Western General Hospital. It was sort of added together. Then the forms were put on one side in the centre.

Q. Yes. You say "... as added retrospectively"; at the time?

A. No, they were added much later, years later. The results that came back from these investigations were accumulated and fed into our computer system, which is where we kept our records.

It was much later in fact, when we were moving hospitals, that we were tidying up and came across a box of these and one of my staff said, "Well, what do we do with these?" I was told all the information was in the computer so should we not just throw them out? And I thought, "Well, it's part of the clinical record, we should put it back in case notes or put it in the case notes," so they were added very much later, about 2003.

Q. 2003?

A. That's when we moved hospitals and we were tidying up and found them.

Q. Why were they not part of the individual patients' case notes from the beginning?

A. Because we had the information on the computer, which is where we kept a lot of the information. And I think --

and they have to be kept, waiting for the results to come back from the Western, they didn't come back at the same time. So they sort of accumulated, I think, in a box.

Then I think, when AIDS became more of an anxiety, or HIV became more of an anxiety, we didn't want to put any information in the case notes -- anything, any hint of HIV or AIDS -- for reasons I have explained in some of the documentation.

Q. Yes.

A. So that's why we kept them out.

Q. Yes. You say when HIV became an anxiety. Is that after patients had tested positive?

A. That was a year or so later.

Q. But is that the period you are talking about --

A. Yes.

Q. -- when you say when HIV became an anxiety?

A. Yes.

Q. Yes, thank you.

A. Yes, when it was known that patients were positive and it became rapidly known within the hospital that there were patients who were testing antibody-positive, we did our utmost to make sure that that sort of information was not in the patients' case notes.

Q. Yes. Thank you. But I think you said that it was later

put back in the records in 2003. Is that right?

A. Yes.

Q. Yes, thank you. Now, could we have [WIT0040800] up? Could we just expand that slightly? We see that that's a document which says:

"Date collected: 11 April 1983."

And reading down a bit:

"Clinical details. AIDS study."

Now, do you recognise that -- or what is that document, Professor Ludlam?

A. This is a request form, a routine request form, used for the haematology laboratory service. You are invited to put in the clinical details where it says, "AIDS study". At the bottom of the form are the patient details. When we receive the sample in the laboratory, we print the result, or write the result, on this request form. That's why, to the left of the clinical details, there are some numbers printed, and if I can draw your attention to the third one down -- it perhaps doesn't reproduce very well, 5.1, that's the total number of white cells. Then you will see, a little further down the 195. That's the platelet count. That had to be done manually. You will see a little below that on the right-hand side, "200 cells", tick. That's to show that 200 cells had been counted for estimating the -- if you

can see these numbers -- neutrophils, lymphocytes, monocytes, eosinophils. There seem to be two counts there.

Q. Is that the "200 all"?

A. That's the 200, yes.

Q. So who has written these entries in the box which starts with "200 all"?

A. That should say "200 cell".

Q. Sorry, "cell".

A. Yes. That would be probably someone in the laboratory because it says "AIDS study" at the top and the writing of "200 cell" looks different from the person who wrote "AIDS study".

Q. So someone in Dr Steel's laboratory?

A. No, this is in the routine haematology laboratory of the Royal Infirmary. This is the form that started off beside the patient.

Q. Right.

A. That went with the patient's blood sample to the laboratory.

Q. Yes. So this doesn't go to Dr Steel then?

A. No, this form came back to us.

Q. Right. I see. So by writing, or by having, "AIDS study" on it, that means that you would know that another sample was going to Dr Steel, so you would get

1 further results?
2 A. No, the same sample.
3 Q. Oh.
4 A. The one sample we processed in our laboratory and then
5 sent on across the town to the Western General Hospital.
6 So there was no extra blood taken for this.
7 Q. Yes. So the same quantity of blood is being analysed in
8 both places. Is that right?
9 A. It's the same sample, yes.
10 Q. Yes.
11 A. There is no extra blood taken.
12 Q. And we see at the bottom left:
13 "Doctor requesting ... "
14 Is that Dr Carr?
15 A. That's Dr Carr, yes.
16 Q. So that's one of your registrars?
17 A. Yes.
18 Q. And do you think that "AIDS study" is his handwriting?
19 A. Yes.
20 Q. So how would Dr Carr come to be asking for these
21 investigations? Would you have discussed it with him
22 beforehand?
23 A. Certainly, yes. We viewed this endeavour as part of our
24 obligation to monitor people with haemophilia. As
25 I explained earlier this morning, it was my

responsibility to monitor patients for side effects of therapy.

Q. Yes.

A. And as immune abnormalities had been demonstrated in apparently well haemophiliacs in the United States, it seemed appropriate that I should assess our patients here in Edinburgh, to see whether they had any immune abnormalities. This was something completely new and important as part of the monitoring process. It was just that.

Q. Yes. We are going to come on to that, Professor Ludlam, but could we have up, please, [WIT0040802]. Could we just go to the top there? Could we expand that a little bit more? That seems to be April 1983, perhaps the 6th? Yes. What is that form, Professor Ludlam?

A. This is a very similar form to the previous one.

Q. Yes. I see that it says:

"AIDS study x 2."

Why does it say "x 2"?

A. I don't know.

Q. You don't know?

A. I don't know.

Q. No. And again, if we go down to the bottom:

"Doctor requesting exam."

A. I think that's Dr Carr.

Q. It's Dr Carr, it is not a "P"? It's "Carr"? It does appear to be different writing.
A. I'm now not quite sure. I think actually this latter one looks a bit more like Dr Carr's writing. I don't know if you want me to go back and comment on the previous one, the writing.
Q. Let's have a quick look at it, yes. It's 0800.
A. With due respect to Dr Carr, I think where it says "AIDS study" at the top, that's perhaps written a little more neatly than he might have written.
Q. Right.
A. I notice this first one -- could you just move it down so I can see the top of it? It's taken at 9 o'clock in the morning and I suspect this was probably an inpatient. I wonder actually whether the form might have been prepared, perhaps, by our haemophilia sister. She had nice neat writing. The blood forms are often prepared the night before for the junior doctor to go round in the morning and she may well have prepared this. It says "requesting doctor" and that would have been Dr Carr, although he didn't actually do it.
Q. I think that might be a good point.
THE CHAIRMAN: Professor James suggests to me that doctors undergo special training in illegibility. So there may be many explanations.

(11.11 am)

(Short break)

(11.39 am)

MR GARDINER: Professor Ludlam, before the break we were talking about samples which had been sent to Dr Steel and we asked you to give us some detail about how this was done. If we go to page 4 of [PEN0120774], the question is, question 6:

"Can you explain what happened (as set out in paragraph 11) more clearly?"

That's a reference back to the other paper where you describe the sample that's taken, and what you say here is that:

"When patients attended the clinic, patients were invited to give a blood sample for the concessions set out in paragraph 6 (as appropriate). In most instances the patient would be invited to lie on the examination couch. A blood pressure cuff would be placed round the upper arm and gently inflated to about 40 mmHg ..."

What's that notation?

A. Millimetres of mercury.

Q. "... to make the veins visible. The skin in the antecubital fossa (flexor surface of the elbow) would be cleaned with antiseptic. A gauge 21 needle would be carefully inserted into the vein and the required volume

of blood sample withdrawn into the syringe."

What's a gauge 21 needle?

A. That's a small needle.

Q. When you say "small", how small?

THE CHAIRMAN: Gauge 21, I think, is the answer to that.

A. There are smaller ones which we use if possible. There are larger ones if you want large volumes of blood. Gauge 21 is the standard one for taking blood samples.

MR GARDINER: Yes, thank you.

A. It's about half a millimetre, I think, across.

Q. Thank you:

"The blood pressure cuff was deflated, the needle removed from the vein and the patient asked to hold a ball of cotton wool firmly on the site of needle entry for five minutes. The needle would be removed from the syringe and blood dispensed into various tubes and the volume of blood would be approximately 15 millilitres, which would be about one tablespoon full."

In the next paragraph you describe how you started looking at lymphocytes and the four to five different types of white cells, and we have looked at that in the other statement. Then the next paragraph we go back to the request forms and you say:

"The labelling of the request forms with 'AIDS study' was unfortunate but was intended as a 'shorthand'

indication to the haematology laboratory that they needed to count twice as many white cells under the microscope and send the sample on to Dr Steel."

Professor Ludlam, why do you say that it was "unfortunate" to use "AIDS study" on these request forms?

A. Well, for two reasons. One is -- in a sense we weren't studying AIDS. This was a shorthand.

Q. I think you had better explain that in a little bit more detail. You said you weren't studying AIDS?

A. We weren't studying AIDS, we were assessing CD4 and CD8 lymphocytes, but we were doing that because of the reports of immune abnormalities in people with haemophilia from the United States, who were well but had abnormal lymphocyte counts.

Q. Yes.

A. And a few patients with haemophilia in the United States developed AIDS.

Q. But it was in connection with --

A. The overall topic, the umbrella topic --

Q. Was AIDS?

A. -- was AIDS, yes.

Q. Yes. Sorry, I interrupted you. You were going on to say?

A. Subsequently it emerged much later on, when one or two

patients asked for their -- copies of their case notes and they saw these report forms in the case notes, they wondered whether, I think, we had undertaken some sort of AIDS -- some sort of different AIDS study, whether we had given people AIDS, whether we had given patients concentrates, clotting factor concentrate, that we knew was infected with an AIDS virus. One story that came to me was that we had put HTLV-III into bottles of clotting factor concentrate, heat-treated them and then gave them to patients to see whether the heat treatment was effective.

Q. Yes. That's why you are saying it was unfortunate that you described this study as an "AIDS study"?

A. Well, when these ideas that patients had -- appear -- the conclusions they appear to have reached or wondered about -- yes, it clearly was unfortunate and perhaps it would have been better to have called it an "immune study".

Q. Yes. Could you help us with the exact procedure that was followed in connection with these AIDS study request forms? You have told us that you asked your staff, your registrar, to collect samples. How was that done with these forms? Just take us step by step through it.

A. The patient would require a full blood count. As part of their monitoring procedure they would have a full

blood count, the chemistry and so on. The request would be sent on the usual request form for the haematology --

Q. Who would send this request?

A. The person who took the blood.

Q. Yes.

A. Yes.

Q. Yes. Do please carry on.

A. The person who took the blood would wrap -- put the tube in a polythene bag along with the request form and put it out for the portering system to collect and take down to the laboratory.

Q. Yes. So from that description, that doesn't sound as though the patient is having anything to do with the request form.

A. The request form is often put down next to the patient and the blood tube is labelled with the patient's name, usually next to the patient. If it's an inpatient, as it appeared one of the samples might have been, the form is taken to the patient's bedside and the tube filled up and put in the polythene bag and sent off down to the lab.

Q. Yes. Okay. Thank you.

A. Or sometimes the blood form would be written by the doctor in the clinic and given to the nurse, who would take the form from the patient and arrange for the blood

sample -- she would take the blood sample.

Q. Just reading on in that paragraph you tell us that:

"When Dr Steel received the samples, his research assistant counted the CD4 and CD8 lymphocytes. The number of each reflected the immune status. At the time we noted gross abnormalities in the patients' immune systems but considered that this probably had nothing to do with AIDS."

We are just a little bit confused about that, Professor Ludlam. How could you know that it had nothing to do with AIDS?

A. I'm sorry. This was a document that was quite difficult actually to put together. It arose, as it says at the top, at a meeting with a member of the team, the Inquiry team, and I wasn't entirely happy with the way it had been recorded what I had said, and I spent a considerable time trying to make it reflect more what I wanted to convey but without deviating too far from the topic. It was a sort of hybrid document that I'm not terribly happy about but I'm very happy to respond to your question.

Q. Is that incorrect, that sentence there? Should we take that out?

A. I think it would be better taken out, yes.

THE CHAIRMAN: Professor Ludlam, you really have to put

something in its place if it's being taken out. This is quite difficult material for you to communicate. It's very difficult for us to take in. But I thought we had spoken earlier about the developing knowledge of these matters, and in your Lancet paper in 1983 you reported these results and I think in that paper there is the expression "Acquired Immune Deficiency Syndrome" as descriptive of the changes in the immune system of the patient. But what we have here is "AIDS" with capital letters, and it is back to the point that I tried to raise with you earlier: whether one has to contrast very carefully Acquired Immune Deficiency Syndromes caused by HTLV-III or another virus and Acquired Immuno-deficiency Syndromes caused simply by the progressive assault upon the immune system of antibodies and other impurities in factor concentrates.

If I have understood that there is that problem, then communicating your evidence becomes a difficult issue but we have to try and get it right. So I think if you could concentrate on giving us preferably a brief statement of the position -- we can get explanations later -- but preferably a brief statement of the position, it might help.

A. I think it would be better if I said at the time we noted gross abnormalities in the patient's immune system

but considered that this was probably nothing to do with an infectious agent causing AIDS."

I think that would be ...

THE CHAIRMAN: So that's the substitute for us.

A. Yes, if I may.

PROFESSOR JAMES: And if I may add, that's the precise conclusion that you reach in that Lancet paper on those immune studies?

A. That's correct.

MR GARDINER: Professor Ludlam, before the break I understood you to suggest that patients involved in this AIDS study knew that they were involved in the study at that time. Is that your position?

A. I'm not sure they all knew. We were keen to involve patients in knowing what we were doing and, as you see, we would have had no inhibitions about writing "AIDS study" on the forms which we would then give to the patients. A little later on -- and I don't know if you are going to come to this -- we did skin testing.

Q. We are going to come to that. I'm just wondering if you are absolutely sure that your patients would see this form. I mean, I would have thought that it would run the risk of alarming them to see "AIDS study" written on their blood sample, particularly if you hadn't talked to them previously about this risk.

A. I think we would have -- I mean, patients knew that I had an interest in monitoring the safety -- a particular interest in monitoring the safety of clotting factor concentrates over the, for example, Hepatitis B situation. When this -- the prospect of this came up, we would have explained to patients what we were doing. There was no secret about it.
Q. Yes.
A. I can't assure you that every patient understood exactly what was done but we were making it clear that we were doing this.
Q. I think you have told us that you were not the only person taking the samples. Did you instruct junior doctors and nurses to advise the patients that the blood was being taken for an AIDS study?
A. We were agreeing what we were doing. It would be part -- we worked as a team.
Q. Yes.
A. And so I think it is very likely that the nurse or doctor -- as you can see, Dr Carr initiated some of these tests. He would have explained what was happening.
Q. I'm going to repeat the question, Professor Ludlam: did you personally instruct junior doctors or nursing staff to advise the patients that they were involved in this

study?

A. I don't know that I would instruct them to tell the patients, but these things were discussed with the patients and they would have -- they might have heard us discussing it.

Q. Yes. So would you accept that it was, in effect, a casual arrangement?

A. It was an informal arrangement. I don't think it was casual.

Q. You see, Professor Ludlam, our information is that, at least some of the patients did not understand that they were being involved in an AIDS study, this kind of research, at that time. Are you surprised about that?

A. No, I'm not. I think it's not always possible to convey this information -- or whatever the information -- to people. They may have forgotten they had been told. We may not have told them. This was part of the monitoring of patients that was my responsibility and -- I mean, if we had asked them exactly what was happening to the full blood counts that we had been doing for years, they might be a bit vague and the same for the chemistry tests, and this was just another test that was important -- it was something, I agree, new, but it was my responsibility to do this and to see what the results were.

Q. I'm going to come to that, Professor Ludlam, but just to try to understand your position about this, is it possible that you may not have told any of the patients that they were involved in this study?
A. No, I think the patients were aware that we were doing immune tests.
Q. The choice of words there: "aware". I'm talking about telling the patient, not the patient becoming aware by indirect means. So following that distinction, is it possible that all of your patients may not have been told that they were involved in this study?
A. It's possible they weren't all told but certainly some were told.
Q. Can you estimate how many?
A. I can't. I would see this as part of the sharing of information of what we were doing, that it was my responsibility to do these tests, that they subsequently assumed much greater importance perhaps than we thought at the time.
Q. Yes.
A. I mean, it was a fairly low grade part of the general monitoring of the patients.
Q. Yes. Thank you. Professor Ludlam, can you help us with this question: how do you think that the patients would see these forms?

A. Well, in the clinic, when the doctor was seeing the patient, they would fill out the forms, they would give the forms to the patients and the patients would then go into another room with the form, give it to the nurse and the blood would be taken. So we were giving the forms to the patients to carry along, and they would sit in a queue, potentially, with the forms in their hands.

Q. So it would be accidental, effectively?

A. Patients actually examine -- if you give them forms, they read them.

Q. I would like to move on to the next question, which is to do with specific consent. That's on page 0778. We have covered some of this but the question is:

"Were samples from all of your patients sent to Dr Steel? If not, how many patients did you take blood samples from which were sent for analysis by Dr Steel to determine the proportion of CD4 and CD8 lymphocytes? How were these patients selected? Did you obtain consent from these patients?"

You answer over the page:

"It is difficult to say that samples from all of my patients were sent to Dr Steel but samples from many patients were sent."

Would you be able to estimate for us what percentage proportion of your patients had samples taken for this

study?

A. Well, it was an ongoing monitoring. So over the next little while, I guess probably 50 or 70 or more.

Q. Per cent?

A. Per cent, yes. Because those were the patients who were coming up.

Q. Yes. Then you say:

"I did not select particular individuals whose blood samples needed to be sent to Dr Steel for analysis. Rather patients were 'self-selected' by being attendees for treatment or review -- people were severe or moderate haemophilia who attended the clinic regularly. I think that the tube was sent from the haematology laboratory to Dr Steel in all instances, where possible, if the haematology request form was labelled 'AIDS study'.

"I did not obtain explicit consent for each individual test from the patients."

Just pausing there, when you say "explicit consent", how would you have obtained explicit consent at that time?

A. I would have said, "This is your routine review appointment and it's important that we monitor, so our usual -- or what we would like to monitor would be your blood count, your liver function tests, your urine

electrolytes, whether you have got an inhibitor to Factor VIII, your virological status." And if we were doing the immune tests, I would have said, "We are doing lymphocyte tests as well".

Q. Yes. That would be how you would obtain explicit consent?

A. That is how I obtain explicit consent, yes.

Q. Then would you record that in the patient's notes as well?

A. No.

Q. No. But you didn't do that?

A. There was implied consent.

Q. Yes.

A. But when a patient came up for their routine visit, they were used to having blood taken for tests that were deemed to be necessary for monitoring their health.

Q. Yes. But you didn't obtain explicit consent. That's what you have told us.

A. I did not go through each individual investigation, like I think I would now. Times have changed and I would very clearly go through -- list the tests in the case notes and make a note that the patient agreed to these investigations.

Q. Yes. Nowadays would the patient usually have to sign a consent form?

A. No.
Q. No. Thank you. Just reading on:
"The tests were seen as part of the general monitoring of patients who were used to blood tests being taken for different monitoring purposes. If a patient did not wish to give a blood sample, then one was not collected. I wasn't trying to keep the immune tests secret but saw them as part of the general monitoring of patients for which we had implied consent."
Would you accept, Professor Ludlam, that these tests were not just part of the general monitoring of patients?
A. No. They were part of -- they became, in 1983, part of the general monitoring of the patients.
Q. Yes, but that's not all they were. General monitoring is concerned with the individual well being of a patient, whereas this has a research dimension, does it not?
A. No, that is a very important point that -- I'm sorry if I have not made it very clear.
These were new tests and they could be viewed as research tests because they were new and there is a completely new situation, a new threat, that it was my responsibility to monitor potential adverse things that

might be happening to patients. That's why we set up these tests with the expectation the results would be normal.

Q. So is it your position, Professor Ludlam, that these investigations were in no way connected with research in connection with the developing investigations into this new syndrome? You talked in your other statement about similar researches in America and so on. It had no research dimension?

A. I don't want to get caught up in semantics but here was a completely new condition that appeared to be, in some parts of the world, a major threat. My responsibility was, as was everyone else grappling with these issues, to use whatever facilities we had available to try and monitor our patients and try and understand how their individual situations were.

Q. Yes.

A. So it's research in that it's new but it's not in a vacuum; it's in the real situation of an unknown -- or relatively unknown -- but appears to be a very serious situation arising and it's the responsibility of those of us who are looking after patients, who potentially are at risk, to do what we can.

Q. So at --

THE CHAIRMAN: Professor Ludlam, I have to confess I'm

having some difficulty with your evidence. I would have thought that there were likely to be more than one dimension to all work of this kind. So far as the individual patient is concerned, one can understand the need to monitor and ensure that any changes in that person's condition were noted and responded to, but the knowledge gained, I might have been inclined to think, had a much wider importance and could potentially at least assist patients and clinicians worldwide in responding to similar situations.

I have to say -- it may be my misunderstanding of things but I would have thought that when one left the care of the individual patient and converted the data into material for general dissemination, it would be impossible to avoid a research component in the work. But have I got that wrong?

A. I think I was reporting the results of my monitoring of the patients.

THE CHAIRMAN: Yes.

A. And that was not only in the 1983/1984 publications, describing these lymphocyte abnormalities, but this stretched on into -- and I'm sure we will come to this later -- the cohort. It was new information that came out of examining the immune systems of these patients. So it was new information. In that sense it was

research but I would call it "new information" -- if I had not published it, it would have been monitoring. I don't see that it necessarily becomes research because I have published it. In a sense it's what we might call these days an "audit".

THE CHAIRMAN: You see, I can understand that there is a distinction. I have seen many letters in the Lancet, the BMJ and others, where a clinician reports an event or a finding and there is no analysis and no discussion. But your papers certainly include analysis, discussion and represent views. So if that's not research, I will have to be asking my university just how they justify their application at the next REF in far greater particularity than I would otherwise. I think you will have to help us to understand why what you were doing was not research.

A. Well, it was research in that I was making available to the wider world the results of the monitoring of our patients.

THE CHAIRMAN: But you called it an "AIDS study", Dr Ludlam.

MR GARDINER: That word is crucial, is it not, Professor Ludlam, "study"?

A. It's investigations that we started in, as you see, in the spring of 1983. In that sense we were studying the patients. We were monitoring them.

Q. "AIDS study"?
A. We went on with the monitoring, as you know, for many years.
Q. Yes, it's the possible disease that is being studied, is it not?
A. That's why the words are unfortunate. It should have been -- what we were doing was studying the immune system.
Q. You see, I'm not trying to catch you out in semantics. It's really a very straightforward question, which is whether this study had a research dimension. Would you say that at that time, when you were doing the study, you had no thought of later publication?
A. Well, we expected the results actually to be normal, not to show any immune abnormality, and that might have been not something we were reporting.
Q. Not worth reporting. Is that what you mean?
A. I suppose it probably would have been worth reporting in contrast to the results that were being reported from elsewhere, if they had been normal.
Q. Can we go back to the paragraph we were just looking at and you say:

"I wasn't trying to keep the immune tests secret but saw them as part of the general monitoring ..."

Professor Ludlam, does this wording that you have

used, "I was not trying to keep ... [a] secret," does that not suggest that you were not telling your patients about this study?

A. No, I have been trying to convey that we had a very open view with our patients about what we were doing, what investigations.

Q. Right. We will just move to the next paragraph, please? You make a comparison between skin tests. You say:

"By comparison, at around the same time we were carrying out skin tests on some of the patients as another immune function measurement."

Perhaps you could just explain to us what that involved?

A. Yes. There are devices called the Multitest device, that's referred to here. It's a commercially produced device that has eight little legs to it, like an octopus. And on the tip of each of these legs is a different antigen, derived from a commonly infectious organism that most of us have been exposed to, for example, one of them is candida, the organism that causes thrush. So these eight -- this device with eight little legs on it is put on the forearm of the subject, pressed on for about 10 seconds and the -- each of these antigens is, as it were, not quite injected but comes in contact with the skin. The patient is then sent away

for a couple of days and brought back two days later and the -- to some of these antigens there will be a response in the skin, a little bit of induration.

This is an immune reaction to, for example, the candida. The immune system recognises the candida and produces a reaction. You measure those and if they are, I think, more than 2 millimetres across, they were said to be positive and you would count up the number of positive scores out of, I think -- there were eight legs. One of them was a control. So I think it was seven out of eight. This was a system for testing the overall effectiveness of the immune system. It was a much more holistic way of testing it than the CD4 and CD8 counts.

Q. Yes. How many of your patients were tested in this way?

A. Probably 20 or 30. That sort of number.

Q. Yes. Were they asked for consent before they did these tests?

A. Yes, this was a research test. This was something that I didn't think was, if you like, specifically related to whatever might be causing AIDS -- AIDS agent. This was a research test. I got ethical approval for it. We explained to patients what we wanted to do. It was, as you see, slightly invasive. It inconvenienced them because they had to come up -- we might have done the

test when they were at the clinic anyway but they had to come back two days later. They were very willing to do this and the results were extremely interesting.

Q. Yes. Can you just briefly describe for us how at that time you obtained ethical approval for this test?

A. I wrote to the ethics committee and explained what I wanted to do and received a positive response that I could do these tests.

Q. Yes. So which committee is this?

A. This would be the Royal Infirmary ethics committee. I think at that stage it was the Royal Infirmary as opposed to the Lothian Health Board.

Q. How many people would be on that committee at that time?

A. I'm sorry, I don't know.

Q. Professor Ludlam, could you explain the difference between carrying out these skin tests that you have just described and carrying out the investigation of immunological abnormality from a consent point of view?

A. The latter test, the skin tests, involved something being done to the patient. It was invasive and therefore -- and it wasn't quite as clear what we might gain out of this. So it was a much more speculative investigation compared with the CD4/CD8 counts.

Q. Who is the "we" in the "we would gain"?

A. Me -- well -- the information, that would be comparable

and have, I think, utility with other published studies; in other words, there was a lot of information about CD4/CD8 counts that one could try and understand but very little, or relatively little, about these skin responses.

Q. Yes.

A. The skin responses were actually -- as I say, much more a speculative test. Therefore, in my vocabulary were much more a research investigation, although actually it turned out to be very interesting. But ...

Q. You do seem to be suggesting that the other studies, at least some of them, that you were doing there had a research aspect to it. You talked about "gaining" from the study. That's not the patients gaining, that's medical knowledge gaining, is it not?

A. Medical knowledge can gain from all sorts of activities that wouldn't be classified as "research". Gathering cases together of particular conditions, for example, drawing generalities out of case histories is not in a sense -- one level is not research; it is describing what has happened.

Q. Well, perhaps we should move on.

You deal with the results of your immune studies at page 3 of [PEN0120351]. This is paragraph 12. So you say:

"From our initial studies in 1983 ..."

This is the AIDS study? You are nodding?

A. Yes.

Q. Thank you.

A. The CD4/CD8 counts.

Q. Yes:

"From our initial studies in 1983 what we observed, to our great surprise, was that the pattern of lymphocyte abnormalities in Edinburgh patients was similar to those in the US; yet none of the individuals had any symptoms or signs suggestive of AIDS. As the majority of patients had only received blood components, or products, prepared from Scottish blood donors, and there were at that time no AIDS cases in Scotland, it seemed rather unlikely that these lymphocyte changes were due to a possible ubiquitous AIDS virus. The cause of the immune changes in the Edinburgh patients was unknown but there were a number of possible explanations related to the underlying condition of haemophilia and its treatment. It was imperative to monitor the patients because if the immune changes were becoming progressively more abnormal there might be a risk of developing opportunistic infections [eg PCP] characteristic of AIDS.

"While contemplating these unexpected lymphocyte

results, a letter appeared in the Lancet highlighting the immune abnormalities in the haemophiliacs in the US and stating that it would be very important to know if similar abnormalities were observed in those with haemophilia treated with blood products collected in a non-AIDS country. As I had such data, it ..."

That's the results of the AIDS study:

" ... it seemed important to submit it for publication because it would offer alternative explanations, other than widespread infection by a putative AIDS virus, for the immune abnormalities observed in US haemophiliacs. This report concluded that the immune changes were likely to be due to 'infusion of foreign protein or a ubiquitous virus rather than a specific AIDS virus'."

That was your conclusion?

A. Yes.

Q. Could we have a look at [LIT0010416]? Is that the publication you are referring to?

A. Yes.

Q. Okay. We see here it's a letter by you, Robert Carr -- who is Sandra Veitch?

A. She was one of our laboratory staff.

Q. And Dr Steel. If we go to the top of the right-hand column, you say:

"We have studied 23 patients with severe haemophilia and von Willebrand disease who have received exclusively SNBTS Factor VIII, Factor IX or cryoprecipitate in the past five years. Most of these patients have never received commercial or non-Scottish Factor VIII. All were clinically well."

You then set out what you found, or what Dr Steel found, and at the bottom we have your conclusion:

"Since there are no known cases of AIDS in our blood donor population, it seems likely that the immuno-suppression observed in haemophiliacs, as reflected by reduced T lymphocyte alpha/suppressor ratios, results from infusion of foreign protein or a ubiquitous virus rather than a specific AIDS virus in the Factor VIII concentrates."

It's the data from 23 patients that you have used for that?

A. Before...

Q. Why was it only 23 patients in the study? Because if you were monitoring all the patients, there must have been many more than that.

A. If you go up to the top of this form -- this page, to look at the date, it was May. We had only just started.

Q. I see.

A. And this would have been sent in probably two or three

weeks before. But seeing as this is up on the screen, I don't know if it's out of order -- the other letter is about haemophilia and tuberculosis. And this was an interesting report in which -- by Dr, now Professor, Hill from Birmingham, demonstrating that children in the Birmingham Children's Hospital, who had been exposed to tuberculosis, if they had haemophilia, had a much higher instance of catching the tuberculosis and this had nothing to do with HIV.

These children were more susceptible to the tuberculosis, irrespective -- as a result of them having been treated for haemophilia, and the further paper for this actually demonstrated that those who had used more Factor VIII concentrate, I think, were at greater risk of tuberculosis.

Q. Yes.

A. This was the preliminary report.

Q. So you would say that that was consistent with the conclusion that you were coming to in this paper?

A. Yes, I think it's very interesting the Lancet put them side by side.

Q. Yes. Thank you.

Your research paper, at the bottom do we see, professor, that this study was supported by a grant from the Scottish Home and Health Department?

A. That was supporting work that Dr Steel had. I don't know what the study was but he had a grant from Scottish Home and Health Department, which was employing the person who did these extra blood tests for us.

Q. Yes.

A. This is a favour on the back of another project that he was doing.

Q. But it wasn't a research study?

A. Well, it wasn't a funded study -- the lymphocyte studies were not a special study from Scottish Home and Health Department.

Q. Thank you. Yes, could we go back to 0353, please? So in the second paragraph of paragraph 13 you say:

"This preliminary report was followed by a more detailed description of our observations. The paper reported that the number of lymphocytes in the blood in Haemophilia A was reduced with a reduction in Th/Ts ratio in half the patients' cells. In those with Haemophilia B the immune changes were less marked, with the number of Th cells being similar to controls, although the ratio of Th/Ts was reduced compared to controls due to higher levels of Ts cells."

Perhaps we could have a look at that, which is [LIT0010425]. Is that the study that you are referring to there?

A. Yes.
Q. Okay. We see the heading:
"Abnormalities of circulating lymphocyte subsets in haemophiliacs in an AIDS-free population."
Who are Edmond and Prescott? Are they doctors as well?
A. Dr Edmond and Dr Peutherer were virologists.
Dr Prescott was a statistician and the others I have described.
Q. Yes. So we see the summary:
"Markers of the immune system were examined in 47 patients with Haemophilia A and B who had been treated exclusively with blood products from a population apparently free from Aquired Immunodeficiency Syndrome (AIDS)."
These 47 patients, do they include the patients in the previous paper?
A. Yes.
Q. If we go over the page, we see that you set out your methods and then the results, then over the page "Discussion". You say:
"Most of the patients reported in this study have been treated exclusively during the past five years with locally prepared blood products and have never received commercial concentrates."

If we just go over the page to the last page, starting at the bottom of the left-hand column, you say:

"The study has not identified the cause of the reduction of Th but it is unlikely to be due to specific AIDS virus in the blood products. It is more likely to result either from an as yet unidentified component of the therapeutic concentrates or from a non-specific effect of foreign protein infused intravenously."

Just pausing there, is that the antigen overload theory, Professor Ludlam?

A. In a nutshell, yes, although the antigens come in many different sorts and may have been cytokines but, yes, it's the non-infectious.

Q. That's the conclusion that you are favouring at this point?

A. Yes.

Q. So reading on:

"Because the reduction in Th is not dose-related and because of its bimodal distribution in patients with Haemophilia A, it seems that some patients are more susceptible to this immunological disturbance than others. What determines an individual's immunological response to transfusion remains elusive. Furthermore, the relation between the lymphocyte subset abnormalities in symptomless haemophiliacs and the likelihood of

eventual frank AIDS remains unclear, although it may be connected with HLA status."

Just in passing, am I right in thinking that these patients remained negative for the virus?

A. They were HTLV-III negative at this --

Q. At this stage?

A. When these samples were analysed -- this is published in June, as you see, 30 June 1984. We now know that unfortunately some of these individuals will have been infected, they are probably part of the cohort.

Q. But from analysing stored samples retrospectively you were able to say that at this point --

A. Not at the point at which these results were acquired.

Q. Yes.

A. Yes.

Q. Thank you. So those were the results of -- or the writing up of the results of the AIDS study.

Can we go to question 8, please? The question is:

"After observing in your initial studies in 1983 that your Edinburgh patients had a pattern of lymphocyte abnormalities, did you advise them of the results of the analysis of their blood?"

Your answer to that is:

"Patients were only advised of any lymphocyte abnormality if they asked."

My question, Professor Ludlam, about that is that surely patients could not ask because they did not know that their blood was being subjected to these investigations?

A. Well, I would beg to differ. I think a lot of patients agree to blood tests for studies and don't come back and ask for the results.

Q. I suppose, certainly you didn't take steps to advise the patients?

A. No, that's correct.

Q. Yes. Why was that?

A. Because we didn't know how to interpret them. This was -- as I have conveyed, I think -- a surprise to us. We were expecting them to be normal and so we were -- for reasons that I think have been laid out already -- perplexed and it didn't seem helpful to go back and pass this information on to the patients.

Q. Thank you. The next question is on page 0781, question 9, and refers back to paragraph 13 that we have just read. It says:

"In paragraph 13 you note that it seemed important to submit your data in respect of immune abnormalities in your haemophilia patients ... for publication because it would offer alternative explanations (other than AIDS) for the immune abnormalities observed in US

haemophiliacs. Your data was published in the Lancet on (1) May 1983 and (2) June 1984. Did you obtain consent from your patients before publishing the results of your investigations of their blood?"

We have answered the next question. So these are the two papers that we have just looked at. That's right, isn't it?

A. Yes.

Q. What's the answer to that? Did you obtain consent from your patients before publishing the results?

A. No.

Q. Why was that?

A. I don't think it would have been necessary. These were anonymised results. It would not have been usual to go back to patients and say, "These are the results, we would like your permission to publish them".

Q. It wasn't usual at that time to --

A. That's correct.

Q. Yes. You said because the data was anonymised. Could you explain a bit more about that?

A. Yes, there was no information in the two publications that we have looked at that would allow the identification of any individual patients.

Q. Yes.

A. It's group data.

Q. At that time, was that an ethical criteria for whether you obtained patients' permission to publish their data?
A. That, I think, came in later. For example, case reports. If I wished to publish a case report now, I would be expected to obtain that patient's consent --
Q. Yes.
A. -- for doing so. But 30 years ago I don't think that would have been the case, even for a case report.
Q. Yes. So -- but 30 years ago, was the fact that the data was anonymised important in determining whether you should publish data without permission?
A. No, I'm just saying it strengthens the case.
Q. Yes. Was that a factor that you took account of at the time?
A. It never occurred to me to get the patient's consent because that was not usual and it was not identifiable, but if I was going to publish a case report, that might be identifiable, then I would share the data with the patient and say, "Could we publish this, please, because it's interesting", and explain why it's interesting.
Q. At that time that's what you would have done?
A. I think I would have done that, yes.
Q. Thank you. Again, you say at the end -- this is over the page -- of your answer:
"Any patient interested in the results would have

been told if they had asked."

Of course, again, it seems that at least some of the patients on your account didn't know. So they couldn't ask, could they?

A. They couldn't ask. They might have heard from other people, if I hadn't told them, that we were doing tests. As I indicated before, there is a very live network amongst patients.

Q. Professor Ludlam, it's clear then that by April 1983 -- we have seen from these request forms -- in fact probably a bit earlier -- you were studying the immune function of your patients in connection with the possible infection with a virus that might lead to AIDS. Would you accept that?

A. Could you just repeat your question?

Q. It's clear from what we have heard this morning that by April 1983 you were studying the immune function of your patients in connection with the possible infection with a virus which might lead to AIDS.

A. No -- oh, well, in connection with -- yes, but I didn't think that our patients had the virus or were at substantial risk of the virus, but in connection with other people's studies, yes.

Q. Well --

THE CHAIRMAN: I think that's now rather confusing. I think

I would have understood that you were studying the deterioration, or what turned out to be the deterioration in the immune status of your patients, which of itself, irrespective of cause, might hypothetically result in an AIDS state at some stage.

A. Yes. A clinical AIDS state.

THE CHAIRMAN: A clinical AIDS state.

A. Yes.

THE CHAIRMAN: So the problem is when one introduces the word "virus" as a cause. I think that's the problem that arose there, Mr Gardiner.

MR GARDINER: But in your study you were allowing for the possibility that the cause was a virus, although that wasn't the theory that you were favouring.

A. Yes.

Q. At this point were you discussing that possibility of infection with your patients and whether they wished to continue with concentrate therapy?

A. No, I don't think so. Because the putative -- we didn't think that our patients were at high risk of the -- of a viral cause for their AIDS in the form of the virus that was over in the United States.

Q. We, the doctors?

A. We, the doctors.

Q. Yes. Even if it had turned out that your favoured

theory of antigen overload was correct, you weren't discussing that possibility with your patients either, were you?

A. No, because it was not clear what should be done if that was the cause.

Q. Thank you.

I want to move away from research and look at testing now for the HTLV-III virus. Can we have a look, please, at page 4 of [PEN0120351]? At paragraph 15. This is the next chapter in the story, if you like, Professor Ludlam. Just reading from paragraph 15:

"By 1984 accumulating evidence indicated that AIDS was probably caused by a virus from blood donors, which was transmitted by clotting factor concentrates. By the autumn of this year, Dr Richard Tedder, at the department of virology at the Middlesex Hospital, had established as a research project, an anti HTLV-III assay. This was an early antibody test, under development, for the detection of antibodies to the putative virus causing AIDS. He only had a limited supply of reagents and he was receiving many requests from other clinicians ..."

Just pausing there, what are the reagents, Professor Ludlam?

A. This would be the virus in order to do the tests. You

would have to propagate the virus. A potentially very dangerous things to be doing. It has got to be done under very carefully controlled conditions, safe conditions.

Q. Would he have received these from Robert Gallo in America? Is that the likely source?

A. I think there were some difficulties in obtaining the virus and I think this may have come from a British isolate. As I'm sure you know, there were difficulties, particularly between Robert Gallo's team and Montagnier's team at the Pasteur, and I think it's possible the initial supply may have come from one of these established labs, but they also had to get -- establish a UK isolate.

Q. Yes.

A. The antibody tests -- they may have got some antibody from one of these two centres, if you like, to authenticate the British isolates. You would need to ask Professor Tedder, I think, about the details of that.

Q. I see that we have covered that in the preliminary report at paragraph 8.23 and we think it's from Dr Gallo. Just reading on there:

"But he agreed [that's Dr Tedder agreed] in October to test serum samples from ten Edinburgh haemophilia

patients. When the results were available, he reported to me that three of the ten were anti HTLV-III positive in his test. Our preliminary conclusion was that it was likely that these patients had been exposed to the putative AIDS virus. This was most unexpected because the patients had only been treated with factor concentrates prepared from plasma collected in Scotland, where at this time there was only one known case of AIDS. To investigate the situation, Dr Tedder agreed to test further samples from other patients. He found that a total of about 20 patients in Edinburgh were apparently anti HTLV-III positive. Preliminary examination of the detailed transfusion records of the patients indicated that the simplest explanation to account for most of those who were anti HTLV-III positive was to conclude that a single batch of concentrate, given to patients in the spring of 1984, was the source of exposure. This was amongst the very first evidence that the UK blood supply had been contaminated by the AIDS virus."

THE CHAIRMAN: It's lunchtime, Mr Gardiner.

MR GARDINER: I'm about to move on.

THE CHAIRMAN: Professor, does the name "Weiss" mean anything to you in the context of producing a British isolate.

A. Robin Weiss? Yes, indeed, we worked with him.
THE CHAIRMAN: I think the impression I have from Professor James is that once Gallo had isolated the virus, Dr Weiss was able to replicate the process here?
A. At the Chester Beatty, I think, yes.
THE CHAIRMAN: But of course, Dr Gallo was particularly keen on preserving his intellectual property rights.
A. I think that that's correct.
THE CHAIRMAN: So things may not have been as open as they might otherwise have been.
A. I think so, yes.
THE CHAIRMAN: We will resume after lunch.
(1.00 pm)
(The short adjournment)
(2.00 pm)
THE CHAIRMAN: Professor Ludlam, can I take up just one small point about language and nomenclature. This morning I was asking you about the description of conditions as "Acquired Immune Deficiency Syndrome". The background to that was a recollection -- let's put it no higher than that -- of an entry in the minutes of the haemophilia reference centre directors, on 13 May 1983. I'll just read out to you what it said:
"Concern was expressed about the definition of 'AIDS'. It was felt that there might be many

individuals with evidence of impaired cell-mediated immunity but only a very small number of these might progress to a full-blown picture of the condition. It is important that such individuals are not classified as suffering from AIDS."

It went on to talk about the importance of opportunistic infections as the diagnostic features.

My impression is that it is about that time that there was an express appreciation that there may have been a looseness in the use of the expression, "Acquired Immune Deficiency Syndrome", prior to that. Is that valid or am I completely mistaken?

A. No, that's completely valid, I think, yes. Thank you for clarifying that.

MR GARDINER: Professor Ludlam, before lunch, we had just looked at your statement where you described testing that had been done by Dr Tedder, if you remember that.

A. Yes.

Q. Could we look at [LIT0011669]. I think the paragraph I read out, you say initially he had reported to you that three patients were anti HTLV-III positive. You said that he found a total of about 20 patients in Edinburgh were apparently anti HTLV-III positive. This article that we see on the screen, what is that?

A. This is the report of the seroconversion of a group of

patients who were exposed to what we believe was a single batch of Scottish -- SNBTS Factor VIII that was transfused in the spring of 1984.

Q. Yes, thank you. So we see from the summary:

"15 haemophiliac patients acquired antibodies to human T-lymphotropic virus type III during 1984 ... A further 18 patients who received the same batch did not seroconvert and one other patient became seropositive but had not received this batch."

So at this stage there were 16 patients who had seroconverted. Is that right?

A. It appears so, yes.

Q. If we go over the page to "Results", the top left-hand column, as you said:

"Between April and October 1984, anti HTLV-III developed in 16 patients with Haemophilia A. The transfusion records of these patients showed that all but one had received a common batch of SNBTS Factor VIII between March and May 1984. Of all the other batches of Factor VIII transfused during this period, the next most likely implicated batch (B) was transfused during January 1984 and was given to only nine of the 16 patients who seroconverted."

Was that the total amount of patients that seroconverted?

A. That was the information that we had when we wrote this, yes.
Q. Subsequently did you have more information?
A. Subsequently further analysis and testing revealed, I think, 18 individuals who we think probably seroconverted from this batch of Factor VIII.
Q. Yes. Are you able to help us with a patient who we understand seroconverted as a result of exposure to the same batch from the Aberdeen haemophilia centre? Is that something that you know about?
A. I know a little about it. I understand there is a patient in -- or was in Aberdeen who received, I think, three bottles of this batch and was subsequently found to be seropositive -- anti HTLV-III seropositive.

I can't recall and I don't know when the last negative, if there was a previous negative result -- and I think there is some uncertainty in my mind -- because I don't have all the details and I'm not sure that in fact all the information can be gathered in. This individual in Aberdeen only received three bottles. Elsewhere in this paper that's up on the screen, you will see that there is a relationship between the number of bottles received and the chance of seroconverting.
Q. Yes.

A. And of those who seroconverted, the lowest number of bottles of Factor VIII, I think, was about ten. This patient in -- and there was a relationship between the number of bottles transfused and the chance of seroconverting.

This patient in Aberdeen only received three bottles and therefore statistically would probably have had a lower chance of seroconverting. That does not mean to say he did not seroconvert to it. I don't have the information available, and I'm not sure that it is available actually, to ascertain whether this was the cause of his seroconversion.

Q. Yes. Thank you.

I would just like to try to get some more information from you about when you received the results from Dr Tedder. If we go to page 9 of [PEN0120774], which is question 10, there is a question there about how you noted that Dr Tedder agreed to test ten patients, he later agreed to test serum samples from other patients. The question is:

"How many patients were tested altogether?"

Can you tell us what your recollection is about that?

A. We sent ten initially and three came back positive in Dr Tedder's test. He then agreed to test further

samples and this -- the figure I have put down here, 50 to 70, I doubt if all those would have been tested in one batch, as it were. He was getting a lot of requests. As we were discussing before lunch, he had limited reagents and there was a bit of congestion in trying to get tests done. These would be done probably over a month or two or three, I would think. I'm just guessing. Of course, we did, early in the New Year of 1984, start to set up a test in Edinburgh and Dr Peutherer in virology and Dr Simmonds set it up.

Q. It would be in 1985?

A. I'm sorry, 1985.

Q. Thank you. Just looking at question 11, this is a question about how you arranged for them to be tested by Dr Tedder. You say that you phoned him and asked if he would test 10 samples. You explained that you had an unusual group of patients in that they had been treated predominantly with NHS concentrate manufactured in Scotland and that you anticipated that they would be negative:

"When he [Dr Tedder] agreed to carry out the testing I would have arranged for the samples to be sent."

Could you just tell us how you did that Professor Ludlam?

A. How I arranged for them to be sent?

Q. Yes.
A. I would have arranged for -- or asked one of my laboratory staff to look out ten samples from the deep freeze, recent samples, from patients with probably severe haemophilia or moderate haemophilia, who had been transfused a lot, to send them to Dr Tedder.
Q. Yes. Before you did that, did you obtain the consent from the patient whose samples you were sending?
A. No.
Q. The next question deals with another aspect of consent. Do you know whether, when the samples were originally taken, the patients were told that they might be used for anti HTLV-III testing?
A. I don't think they would have been told because we had no idea when the testing would become available, that a viral aetiology would be forthcoming. And these were samples that were laid down, as I have indicated previously, periodically when patients attended.
Q. Yes. When do you think it was that you received the results from Dr Tedder?
A. The initial results, I think, were received on 26 October 1984.
Q. Yes. How did you receive them?
A. By telephone call.
Q. We see at question 13, if we could just have page 2 of

[DHF0025363] up, and if we could see the first page there, this is the Central Committee for Research and Development in Blood Transfusion. If we look at the next page in the middle, just above paragraph 8.3, it says:

"... [it has been redacted] referred to a batch of Factor VIII in Scotland, fractionated in November 1983, which was discovered to contain anti HTLV-III in August 1984."

So that suggests that it was earlier than October. What do you think about that, Professor Ludlam?

A. I think this is mistaken text on two grounds: first of all, the antibody tests were later than August 1984 but I think, more importantly, it says that:

"... the Factor VIII in Scotland, fractionated in November 1983, which was with discovered to contain anti HTLV-III ..."

Well, the Factor VIII batch, the implicated batch, as far as I know, has never been found to have anti HTLV-III in it -- as far as I'm aware.

Q. Yes. Thank you.

A. I wasn't at this meeting. I know all the names are redacted but it wasn't a meeting I was at.

Q. I wonder if we could have a look at [PEN0120526].

This is an excerpt from the transcript of the

evidence of Professor Tedder to the Lindsay Tribunal on 9 July 2001 and you will see there, Professor Ludlam, in the second paragraph:

"I see. When did this first come to light, this outbreak, as a result of Scottish product; I think you give March 1985?

"Answer: I think it was earlier than that. I think it was -- I mean, March 1985 was the description of one of the young men who developed glandular fever-like illness, but I think this was predated by a discussion with Christopher Ludlam; I think it must have been in late autumn 1984 when we did the first testing for him, because it was -- it was certainly -- I will never forget. It was sitting in what used to be David Danes' room at the end of the corridor, looking out on an autumn sun which was a very hot sort of Indian evening, Indian summer evening, which should have been a lovely evening. It was about half past 7:00, 8:00, going through this litany of positive, positive, positive. And Christopher Ludlam obviously getting more and more pensive and me feeling less and less kind, as this evolution of damage done to a cohort evolved. That was the very early testing when he had sent us cohorts of samples which he already had a clinical suspicion that something had occurred, and that was the beginning of

the evolution of knowledge on the Edinburgh cohort."

We don't have Dr Tedder here but he seems to be talking about giving you results for more than three positive tests.

A. No, he said, "positive, positive, positive," there are three positives there. There were only three. He and I both remember this conversation very vividly and it was at about 8 o'clock in the evening. He rang me at home. So there were only three in the first ...

Q. Yes. Okay. Let's have a look --

A. Sorry, did you want to -- the question about my having suspected that there was something not quite right.

Q. Yes, we can deal with that. Perhaps you could explain that. Yes, your clinical suspicion?

A. I don't think that is actually correct. I think that is Dr Tedder surmising from what emerged later. We had a young man who had a very routine, straightforward operation in February -- sorry, in March -- I think March and April 1984 -- and became exceedingly ill and looked like he had got acute leukaemia. He didn't have that. It was very, very distressing for everybody. He was very ill. We had no idea what was wrong with him. Fortunately, he got through, recovered. We had stored samples on him because we had no idea. This was something completely new and when the --

Dr Tedder's test became available, we just wondered whether this was a strange manifestation of HIV and the -- Dr Tedder showed that antibodies appeared half or two thirds of the way through this unfortunate young man's clinical episode.

This was the first recording, we think, of what came to be known as the glandular fever illness, and we wrote it up because it was very important observation.

Q. But you think that Dr Tedder is wrong to say that you had a suspicion before you received the results?

A. I think so. I think he is thinking -- as it were -- with the knowledge then of a glandular fever illness that we had shown the seroconversion on.

Q. Yes. Perhaps we could just have [LIT0010894] up, please. Is that the case report of what you have just described?

A. Yes.

Q. Thank you. Just looking at question 14. This is still on Dr Tedder's advice about results. The question is:

"When were you advised about the results of the first batch of ten patients? How were you advised?

"Answer: Dr Tedder telephoned me at my home one evening at about 8 pm. I think this occurred some time in October 1984. Evidence given by Dr Perrie shows that the date was 26 October 1984."

What evidence are you referring to there, Professor Ludlam?

A. I got a little confused, but when Gemma Lovell and Mr Douglas Tullis came to see me or we had the meeting, it gave rise to this document. They brought what I thought was a transcript from the Lindsay Inquiry with this date in. I was subsequently reassured I had misunderstood the document. I wasn't left with it. It was just passed across the table to me and taken away again. So that was my confusion. I had misunderstood because we had been discussing Dr Tedder's contribution to the Lindsay Inquiry in the preceding minute.

Q. Yes. So you say:

"The initial notification tests, SNBTS, was when I telephoned Dr Brian McClelland on the evening of 26 October 1984."

How have you arrived at the date of 26 October?

A. Because that was the date of the document that was shown to me.

Q. So we should take that out?

A. I think -- just go back a page. It says:

"Dr Perrie shows that the date was 26 October ..."

Q. So you are relying on Dr Perrie there?

A. I was.

Q. Yes.

A. But it was round about then, if I can say. It was late October.

Q. Your own estimate is late October?

A. Yes.

Q. You say that you told Dr McClelland straight away?

A. Yes.

Q. I just want to show you a supplementary statement that we have received very recently from Dr McClelland, which is [PEN0121426].

You see the fourth paragraph down:

"Dr Christopher Ludlam telephoned me at home on the evening of Friday October 26 to let me know there were six of his patients who had been found to have developed antibodies to HTLV-III on initial testing."

So he is remembering it as six.

A. My memory is of three.

Q. Yes.

A. It's 30 years ago. I'm sorry -- I'm sure he will say it's six and I'll say it's three. I'm fairly certain it was only three but I might be wrong.

Q. Yes, thank you. He seems to be distinguishing between patients who had been treated with commercial concentrates, as opposed to SNBTS. The first three that you heard about, were they patients that had, to your recollection, had only received SNBTS product?

A. Yes, I think I had sent in Dr Tedder specifically ten samples from people who had only received SNBTS and that equates with, I think, the fifth or sixth line down in this paragraph:

"Dr Ludlam thought that in three of these patients seroconversion probably attributed to SNBTS product."

Q. Yes. Could we go back to the notes and look at question 16? This is about who else you told when you received the results. Do you remember who else you told, Professor Ludlam, other than Dr McClelland?

A. I would have informed Professor Bloom, as chairman of UKHCDO, because this was a devastating observation. Assuming that I could rely upon Dr Tedder's test. Dr Tedder's test was a very new test and there was the -- I think he would be prepared to say there might be false positives and false negatives, and maybe we will come on to discuss this later. But I had to take these results and assume that they were true.

Q. Yes.

A. This was the first, I think, confirmed case of seroconversion to a UK blood product. There had been cases -- one or two cases in England of batches of concentrate in which a donor who had donated in all good faith developed AIDS after having donated. The batch of plasma was processed. Made into Factor VIII and then

given to patients, some of whom were then found to be anti HTLV-III positive but it wasn't certain that it was acquired from that batch. This was the sort of work that Dr Craske was very methodically and carefully trying to elucidate what was going on, but this was amongst -- if I can put it that way -- amongst the first information that there was HIV in the British blood supply.

Q. Yes. How did you personally react to this news, Professor Ludlam?

A. I was horrified. It was awful.

Q. Were you surprised?

A. I was devastated.

Q. Was there anybody else that you informed?

A. I told Dr Peutherer, our local virologist, and I told Dr Craske because he was designated to help with these sort of investigations and monitor the situation for UKHCDO.

Q. Yes. We should have a look at [PEN0120857].

Sir, we have written to Dr Peutherer about this and you will see that he says:

"I first became aware that Edinburgh haemophiliacs had been shown to be infected with HTLV-III soon after Dr Ludlam was informed of the results by Dr Tedder. Dr Ludlam spoke to me about the results. I do not know

how Dr Ludlam was informed."

Then:

"Subsequent testing, I think testing for HTLV-III infection, started in 1985, once commercial tests became available. All testing for patients from RIE carried out by the Hepatitis B and HTLV-III HIV reference lab within the virus diagnostic service of university department of medical microbiology in the medical school, Teviot Place, and the tests used were purchased from several companies, Abbott, Wellcome and Ortho Labs."

Just while we are on that, Professor Ludlam, when would these commercial tests first become available to your recollection?

A. There were different tests being developed of different degrees of specificity and sensitivity. They were developed over late 1984 and 1985. I'm not an authority on them. The blood transfusion virological experts and Dr Peutherer would give you a much more informed response than I can.

Q. Yes.

A. But a huge amount of work went into trying to get a sensitive and specific test so there weren't too many false positives and false negatives.

Q. Did you have occasion to use the commercial tests

subsequently?
A. No -- I personally didn't, no, not in my laboratory, no. The samples -- if I wanted samples testing, once reliable testing was available in Edinburgh, I sent them to Dr Peutherer.
Q. Yes, I see.
THE CHAIRMAN: Professor Ludlam, Dr Winter, who gave us evidence earlier, told us that Dr Kernoff had his results in October of the first testing and said that he himself, Dr Winter, received the results of Dr Tedder's testing for his centre on 26 October 1984. Is there likely to be any significance in coincidence of dates around about this time, do you think?
A. I think a lot of haemophilia physicians were keen to get patients tested. There had been so much uncertainty.
THE CHAIRMAN: I was thinking of it from Dr Tedder's point of view and whether he would be testing in batches.
A. Almost certainly. He might have been doing a batch every day or two because there were, I guess, hundreds of samples coming in.
MR GARDINER: Thank you, sir.
The samples that were sent to Dr Tedder, were they labelled with the names of your patients?
A. Yes.
Q. I think in answer to question 17, you talk about

transcription errors. Could you maybe just explain what that concern was?

A. Yes. If identifying details about a patient, either their name or a number or an initial or a date -- every time it is written there is a finite chance there will be a mistake, and you have got a row of tubes in a rack and someone is writing numbers, for example, on them. It is very easy indeed to get numbers a bit confused, not to remember to up to the next number when you number the next tube. So if you write a name, it is rather more specific and is probably less likely to result in error.

Q. Yes. Thank you.

A. It is a common difficulty in running laboratories.

Q. Yes. Thank you. In the answer to question 18 you explain that a further lot of samples, you think, were sent down to Dr Tedder. When do you think they were sent down?

A. I have said a few days, and I think we were keen to know more about what the situation was with our patients.

Q. Yes. Thank you. I would like to ask you a little bit about the treatment that these patients that had tested positive had received previously. Could we have [PEN0120159]. And Professor Ludlam, there is a hard copy just in front of you. This is the spreadsheet.

It's just in front of you there.
A. Thank you.
Q. Sir, there is a copy to your right.
THE CHAIRMAN: Do I have to read more than one sheet together?
MR GARDINER: The other copy was for Professor James.
On the sheet that's in front of you, Professor Ludlam, I have noted on it five numbers, patients, 5, 16, 19, 21, 22, not included in the Edinburgh cohort, and I think that's what you told us when you were here previously. Is that right?
A. I assume so. I can't check the numbers. I assume you have got them correct.
Q. Thank you. We don't need to hear in detail but could you broadly describe what treatment these patients had been receiving?
THE CHAIRMAN: That's the specific numbers?
A. The five numbers?
MR GARDINER: Actually --
A. Or the other --
Q. Excluding these five?
A. Excluding the five. Yes, they had been treated with predominantly SNBTS Factor VIII concentrate or cryoprecipitate.
Q. Yes. Is it predominantly or exclusively?

A. Predominantly.
Q. Predominantly?
A. Because you will see patient E1 received some Cutter Factor VIII.
Q. Yes. Yes, Cutter?
A. Yes.
Q. Yes. Thank you. These people with haemophilia, were they severe or mild? What was their condition?
A. It is actually on the table and I think they all have severe haemophilia. It's in the third column across.
Q. Yes. These are the members of the Edinburgh cohort.
A. The ones excluding these five that you have put on the side of the table. Yes.
Q. Yes. Thank you.
THE CHAIRMAN: I wonder if I could just try clarify in my own mind the background of the people. Were all of the members of the Edinburgh cohort members of the study group when you were looking at immune deficiency generally? Or were there differences?
A. I think the majority of them had had their immune function assessed at some stage prior to being exposed to HTLV-III in the spring of 1984.
THE CHAIRMAN: Right. So even if they weren't particularly in the earlier study, they had all been looked at from that point of view?

A. It was part of our monitoring process. So the net would have been spread wider. So we would probably have assessed the immune -- the CD4/CD8 counts in the majority of the people in the cohort. I think somewhere in one of the publications -- I don't know if you are going to come on to them -- this may be spelt out how many.

THE CHAIRMAN: I'm just trying to get a general picture at the moment. If we take E1 for example, on that basis, then there is a great history of treatment down to 1982 and 1983, and there must have been a point within that sort of period, 1983/1984, when the individual was infected, not having been infected before.

A. Yes.

THE CHAIRMAN: Are there any generalisations that one can apply in looking at this table or is it necessary to look at every case individually to form a view?

A. I'm sorry, a view about?

THE CHAIRMAN: Date of infection. We go back to your other data for that?

A. We have to go back to the -- two things. One is the transfusion records and the other is the last seronegative sample and the first seropositive. And it was those two that allowed us -- those two bits of information that allowed us to pin down that this was

the most likely batch of Factor VIII.

THE CHAIRMAN: But if we just take this particular example, in 1982 and 1983, "commercial product" shows twice.

A. Yes.

THE CHAIRMAN: Then it's the last two in 1983 and 1984 that record PFC Factor VIII.

A. Yes.

THE CHAIRMAN: Yes.

A. But we almost certainly know that he was anti HTLV-III negative in early 1983. I'm sorry, 1984.

THE CHAIRMAN: 1984.

A. 1984, yes, I'm sorry.

THE CHAIRMAN: So you had the information available. We will look at the findings in detail in due course. You had the information in this case that would enable you to exclude the Koate as the causative factor.

A. Yes.

THE CHAIRMAN: I see, thank you.

MR GARDINER: Thank you.

A. In fact this information is in the paper that we reported -- that you showed us a movement ago from the Lancet in March or May 1985. It gives the time of the last negative and the first positive for every patient.

THE CHAIRMAN: I will have to work it out in due course but I can't carry all of that in my head all the time,

professor.

MR GARDINER: Of course, on the spreadsheet we do have a column which gives us the date of the last negative test.

THE CHAIRMAN: Oh, yes. Thank you very much.

MR GARDINER: It's not very easy to read this spreadsheet sir, it must be said, but --

A. I think this one was last negative in August 1984. So quite a long time probably from when he was exposed to the concentrate, before he seroconverted.

Q. Yes, indeed. Thank you.

Sir, unless you have any more questions about the spreadsheet, I propose to put that away.

THE CHAIRMAN: At the moment I'm inclined to ask whether it could be filleted so that it only contained the relevant data and not a great mass of irrelevant material from before. I think that would help everyone, if we reduced it to the timeframe that mattered. I'm not suggesting we dispose of the totality but just a little summary of the critical factors might help me, at least to identify the significant part. I think we can do that in-house, as it were.

MR GARDINER: Yes, indeed, thank you, sir.

Professor Ludlam, I would like now to talk about the meeting in December 1984, and there is a question about

it, which starts on page 13 of the notes:

"What was the purpose of the meeting on 19 December 1984?"

Perhaps you can just tell us at the moment what the purpose was, as far as you can recollect.

A. Perhaps I can provide a little background. As a result of my observations of these seroconversions, demonstrating that there was HIV in the British blood supply, this was one of the major factors that led to the meeting on 10 December at Elstree, between senior staff in National Blood Transfusion Service for England and SNBTS for Scotland, along with the protein fractionators from BPL and PFC and haemophilia directors. That was a very long and a very difficult meeting and was set up to discuss where we should go from here in relation to treatment of haemophilia in the UK.

Q. Maybe we should have those minutes up. [SNF0013850], please. That is the meeting you are referring to, is it?

A. Yes.

Q. We see there that Professor Bloom was present, Dr Kernoff, Dr Jones and yourself, of course, Dr Cash, Dr Craske, Dr Forbes, Dr Savage, Dr Tedder, all of these names that we have heard about.

I'm sorry, I interrupted you, professor, please carry on.

A. At this meeting I described what had been found in Edinburgh, and Dr Craske described his activities and what he had found out from various, or a couple of what appeared to be batches that may have been infected.

There was a lot of discussion, both about testing but also whether we should move over to heat treatment. There was a long discussion about the heat treatment and some of us were very concerned about the potential for it damaging the Factor VIII molecule, giving rise to antibodies that then might make the patient untreatable for their bleeding disorder, versus the evidence that had come to light in, I think it was, October of that year, of 1984, that maybe retroviruses were very heat sensitive.

There was a long -- very painful -- discussion and it was eventually agreed that it probably would be prudent to move towards -- to change over to heat treatment if possible. But it was not an easy decision and had it not been for one or two people with fairly strong views at the meeting, we might not have moved over. That would have had very major implications the world over because many other countries started to heat-treat after the decision was made in the UK.

Q. I see. I think you were giving us that background to answering the question about the purpose of the December meeting?

A. Yes. We had this very long meeting, some of which I remember well, and I came back to Edinburgh at the end of a very long day, and I think it was the following day or it might have been the day after that, I was phoned up by a reporter from the Yorkshire Post, who seemed to have all the details that I had about what was then known about the seroconversions in Edinburgh. He wanted to come and see me about it and he wanted to publish it.

So I agreed to see him and he came up to see me, probably the following day again, and I begged him not to publish it because this was no way for our patients to discover what had been happening.

He was very keen to publish. He thought it was a scoop and I had to negotiate fairly hard with him for him to delay a week, and I promised him that this information, as far as I was concerned, would not go out to any other newspaper. It would give us time to organise a meeting for the patients.

So that's when we wrote rapidly round to all the patients, I think, in Scotland. And I think some of the documentation you have from the Scottish Office indicates that it was a meeting to which all patients in

Scotland were invited, although I think predominantly the ones came from Edinburgh and Glasgow. I'm sorry, I don't have a copy of the letter. That's lost. But we did mention in the letter that it was a meeting about AIDS and that's why I expected large numbers of people to come.

That's why the meeting was set up. We thought this was the quickest and most open way to start to inform the patients.

Q. How many letters were sent from the Edinburgh Haemophilia Centre as far as you can remember?

A. We would have sent the letter to all our registered patients. That would be a couple of hundred probably.

Q. Yes. Do you remember what the arrangements were about patients elsewhere in the country receiving letters?

A. Yes, they were sent out, as far as I recall, from each of the other haemophilia centres from Glasgow Royal Infirmary, I assume, Yorkhill, Dundee, Aberdeen and Inverness.

Q. Who organised that?

A. I can't remember. I suspect I did. I, I'm sure, drafted the letter and I probably sent it or -- I can't remember whether there were faxes in those days. I might have faxed it to the other East Coast centres and said, "This is what we are sending out, could you

send out something similar."

Q. Yes. So that was a request to send out letters in the form that you had drafted. To your personal knowledge were any such letters sent out by other centres?

A. I assume they were. I have not heard they weren't. I assume they were sent out.

Q. I'm sorry to press you, Professor Ludlam, but what's the basis for your assumption about that?

A. I would have discussed it with the directors of those centres and asked them to send it out.

Q. Yes. So who were the directors at that time?

A. Dr Tudhope in Dundee.

Q. Dr Who, sorry?

A. T-U-D-H-O-P-E. Dr Audrey Dawson in Aberdeen and Dr Cook in Inverness.

Q. So did you contact them?

A. That's what I'm sure I would have done, yes.

Q. You say "would have done". That suggests that you don't have a memory of doing it?

A. I don't remember but this was an important meeting that we wanted to invite everyone in Scotland to and I would have done that by phoning up these co-directors and asking if they would notify people of the meeting that we were holding in Edinburgh.

Q. Yes.

A. Because, it was of some importance that patients were notified because the Yorkshire Post was going to publish, on 20 December, its article.
Q. Yes. So you said "we wanted to". Who are you referring to there?
A. I think principally myself and probably Dr Forbes.
Q. Yes. So did you discuss this plan with Dr Forbes?
A. Oh, yes.
Q. Yes. What did he say about it?
A. He thought it a good idea. I can't remember who initiated -- I must have initiated the discussion because I was the one who had been visited by the Yorkshire Post. So I would have phoned -- I'm sure I phoned Dr Forbes and said, you know, "What about holding a meeting?" which he thought was a good idea and so we laid the plans.
Q. Yes. What was the arrangement with letters to his patients. Do you remember?
A. He was going to write to them. I would have given him the details of the venue and he would write to them.
Q. So you didn't provide him with a copy of the letter that you had drafted?
A. I'm sorry, I can't remember. I might have done. We were keen to get it out quickly. It might have been I dictated over the phone to him. It just needed to be

a short letter. I can't remember the mechanics of it.

Q. It might seem like an obvious question, Professor Ludlam, but why was it so important that you had a meeting with the patients before the story appeared in the press?

A. Well, I think it's more appropriate for this very unexpected finding to be conveyed by the physicians, by the doctors looking after the patients, than reading it in the newspapers.

Q. So by the time of the meeting you had had the results for, what, just under two months?

A. Just under two months, yes.

Q. Just under two months?

A. Yes.

Q. Before the Yorkshire Post got in touch with you, what steps had been taken to inform the patients?

A. We hadn't taken any steps because we were still assessing the situation.

Q. I think it might be time for a break.

THE CHAIRMAN: We will have short break as usual for the stenographer.

(3.11 pm)

(Short break)

(3.23 pm)

THE CHAIRMAN: Yes, Mr Gardiner?

MR GARDINER: Thank you. Professor Ludlam, before the break you told us that the catalyst for the December meeting was the Yorkshire Post journalist and if you look at page 14 of the notes, at the top of the page, what you say there is that:

"The purpose of the meeting was to inform patients that HTLV-III tests had been carried out and that some patients were positive for HTLV-III antibody and to tell patients what we knew about AIDS."

You don't mention the Yorkshire Post there. Could you tell us why your answer has changed?

A. Well, in a sense the purpose of the meeting was to inform patients about HTLV-III and AIDS and the testing. What I offered you before the break was some of the background, which is, if you like, the timing of the meeting.

Q. Yes. Would I be right in thinking that if the Yorkshire Post had not had this interest in this story, this meeting would not have taken place at the end of December 1984?

A. I think we would have devised another means by which patients would have been informed.

Q. Yes.

A. This would not be my first choice, given a completely blank sheet and without other constraints.

Q. Yes. Why not?
A. It's a very public place, a meeting. People might be quite anxious about what was being said, quite concerned, and there is not much privacy in a meeting with lots of other people.
Q. So from a patient's point of view, it is not ideal?
A. That's correct.
Q. Thank you. We had a little discussion about the letters that were sent inviting patients to the meeting. Are there any copies of this letter anywhere, as far as you know?
A. Not that I know of.
Q. Yes. Were file copies of the letter placed on the files of your patients?
A. No. Not of the invitation of the meeting.
Q. We have some documents from that era, Professor Ludlam, to look at. Could we first of all look at [SGH0026545]? If we look at the bottom of that minute, you see that the date is 20 November 1984 and this is a minute from Hugh Morison to private secretary and Mr Mackay, health minister. The heading is "Blood transfusion:AIDS". It says:

"Ministers will have seen reports in the press about the recent death of a haemophiliac who had been treated with imported Factor VIII, and about the DHSS proposals

to issue a revised leaflet on AIDS to blood donors which will make it clear that all practising homosexuals, and not simply promiscuous homosexuals should not donate blood.

"In Scotland, a revised leaflet was prepared by the Scottish National Blood Transfusion Service in August. This has been sent to all donors receiving mailed reminders to give blood apart from those in the West of Scotland. Steps are now being urgently taken to issue it to donors in the West of Scotland, and to those throughout Scotland who do not receive mailed reminders -- for example students, who simply turn up to a donor centre in response to generalised publicity. Communication with the donor population in Scotland with regard to AIDS is therefore well advanced. In addition, the SNBTS is considering whether the present arrangements can be tightened up still further, for example, by asking donors to sign a declaration before giving blood that they are not among the at risk categories."

Then this is the interesting part for our purposes:

"A development of particular concern in Scotland is that 16 Scottish haemophiliacs have been identified as having antibodies to the virus HTLV-III, which is implicated with AIDS. The presence of the antibodies

indicates that the patients have been exposed to the virus but does not mean that they will necessarily develop AIDS. A batch of Factor VIII, the blood clotting agent given to haemophiliacs, produced at the protein fractionation centre at Liberton, appears to be implicated. As Factor VIII is produced from plasma recovered from blood donations, it must be assumed as probable that the batch was contaminate by a Scottish donor. The batch has been withdrawn and the SNBTS are taking vigorous steps to identify the source of infection. This, however, will not be an easy task since blood from many donors is used to produce a single batch of Factor VIII. In the meantime work is urgently proceeding to introduce the heat treatment for Factor VIII in order to kill the virus and to develop a screening test for HTLV-III antibodies. No such test is, however, likely to be readily available in the immediate future."

The final paragraph:

"It would not be appropriate at this stage to issue any statement on the discovery of the antibodies in the Scottish haemophiliacs. Suitable defensive briefing has, however, been given to SIO."

We see at the top the minister's handwritten note, which says:

"Thanks. While I fully appreciate that a statement would give rise to great concern among haemophiliacs, and indeed among recipients of blood generally, I do not want us to be accused of a cover-up. If we are approached we must be perfectly open. When is heat treatment likely to be ready?"

Professor Ludlam, were you aware of these sorts of discussions going on at this time?

A. I hadn't seen this document.

Q. You hadn't?

A. I hadn't seen this document until it was sent round with the papers for this session.

Q. Yes. Perhaps we could go to [SGH0026503]. If we go down to the bottom, this is a minute that's dated 12 December 1984 from Dr Bell to Mr Davies and Mr Hoy, copied to Dr McIntyre and Mr Murray:

"Haemophiliacs with antibodies HTLV-III. I had phone calls last night from Dr McClelland, Dr Ludlam and Dr Cash (in that order), letting me know that there is likely to be publicity in the Yorkshire Post tomorrow relating to the Edinburgh haemophiliacs with HTLV-III antibodies attributable to contamination of a Scottish batch of Factor VIII. It has to be presumed that this has been leaked by one of the English haemophilia directors involved in last Monday's meeting of the UK

haemophilia reference centre directors."

That's the meeting you referred us to earlier, isn't it?

A. It is.

Q. "One of Lothian Health Board's press officers has been in touch with SIO. You may wish to discuss what should be the department's response to this development.
I understand that Dr Cash has also spoken to you direct.
Since dictating the above, Dr Ludlam has informed me that the Yorkshire Post journalist has agreed to postpone his report until Thursday, 20 December. This will enable the haemophilia consultants to call a meeting of haemophilia patients to explain the situation. In view of this development, I advise that SHHD should not publicise this matter before the patients themselves have been informed professionally. It would be important for Dr Ludlam to be able to assure the journalist as soon as possible that we do not intend to anticipate his publication."

So how does this fit in with what you told us earlier about your discussions with the journalist? Is this just after you have negotiated an extension?

A. I think so, yes. It sounds like the 12 December was probably the day I negotiated the extension.

Q. Yes.

A. Otherwise it would have come out on the 13th.
Q. Yes. I see that in the minute it's put that:
"This will enable the haemophilia consultants to call a meeting of haemophilia patients to explain the situation."
I just wondered, Professor Ludlam, just to be absolutely clear, whose idea was it to have this meeting?
A. I think it was mine. I'll take ownership and responsibility for it. And the fact we held it in Edinburgh rather suggests that it was my idea.
Q. Yes.
A. I think it probably was my idea.
Q. Yes. Yes. It looks perhaps that you have told Dr Bell on the phone that this is the plan.
A. It looks like it, doesn't it, yes.
Q. You have told us already but this minute really makes it clear that the main driver for having this meeting in December is the Yorkshire Post's interest in the story.
A. Yes. What I'm uncertain about in this letter is the last sentence, the first paragraph:
"It is presumed that this was leaked by one of the English haemophilia directors ..."
I don't know who leaked this information. There

were, as you saw, a lot of people at the meeting. There were some haemophilia directors, there were a whole range of people. I suppose it could have been any of them.

Q. Yes, of course.

THE CHAIRMAN: The minute seems to be quite clearly in two parts, Professor Ludlam. The first paragraph narrating fact, the second really putting it in the hands of the department to decide on the response, and then the third paragraph begins with:

"Since dictating the above, Dr Ludlam has informed me ..."

And at this stage Bert Bell is prepared to give some advice. Do you remember speaking to Dr Bell a second time?

A. I'm sorry, I don't but I might well have done. I was clearly very concerned and was telephoning a number of people. I may well have telephoned Bert Bell on two occasions.

Q. Thank you. Could we look at [SGH0026498]? This is another government minute and this one is dated 19 December 1984, from Mr Davies, who we think is a civil servant, to the private secretary to the health minister, John MacKay. The heading is "AIDS":

"I refer to your minute of 12 December. A meeting

of Scottish haemophiliac patients is being held this evening at which the position is to be explained to them. We now understand that 15 not, as hitherto thought, 16 patients treated with Scottish produced Factor VIII have antibodies to HTLV-III. The Yorkshire Post article is expected tomorrow. A copy of a draft press release, agreed with medical interests and SIO, is attached. SIO intend to issue it at noon tomorrow."

Professor Ludlam, that is why we are fairly confident that the meeting took place on 19 December 1984. Would you agree with that?

A. Entirely.

Q. Yes, thank you. If we go to [SGH0026491], we see that that is indeed the Yorkshire Post article but do you recognise it?

A. Yes.

Q. Thank you. Do you remember when it appeared, Professor Ludlam?

A. I think it was Thursday, 20 December.

Q. The following day?

A. Yes, I think so.

Q. Thank you. Yes, it says "Thursday". Thank you.

Just to get a little bit more detail about the arrangements for the meeting, could we go to the notes

at page 14? This is question 20:

"Why was there representation from Glasgow at the meeting? (that is, why was Professor Forbes ... in attendance and why did he chair the meeting)?"

Perhaps you can just tell us, Professor Ludlam, why Professor Forbes was there?

A. We had invited all patients with haemophilia to the meeting, and to bring a friend or spouse as well. There were anti HTLV-III positive patients known of in Glasgow and in Edinburgh and it seemed only appropriate that Dr Forbes should come. He was my senior colleague and I therefore suggested that -- or we agreed that he should chair the meeting and introduce us.

Q. Yes. Professor Forbes told us that he wasn't sure why he had been invited to go to the meeting. Can you explain that?

A. I can't, except with the passage of time that he is a little older than me and his memory is failing as fast -- almost as mine is.

Q. You told us a little bit about the letter that you sent inviting people. I wonder, could I get a little bit more detail about it? You said that it was:

"Inviting people to a meeting in connection with AIDS."

Is that right?

A. Yes.
Q. Did it say much more than that?
A. I can't remember but I remember being very keen to put "AIDS" -- the word "AIDS" and "Acquired Immuno-deficiency" in the letter to attract people to come.
Q. Yes.
A. I thought a lot of people might come. As you know, there are about 400 people with haemophilia in Scotland and if each brought a friend, relative or spouse, that was potentially 800 people.
Q. Yes.
A. I had reserved two large lecture theatres, anticipating that we might get a large number of people and if we had have done so, Dr Forbes would have spoken in one and I would have spoken in the other, and Dr McClelland would have spoken in both.
Q. Yes, I see.
A. But we had a smaller number. So they all fitted into the large surgical lecture theatre in the Royal Infirmary.
Q. What was the tone of the letter? Was it an urgent communication? I'm trying to get a feel for what the letter communicated?
A. I think we would have said:

"New information has become available about AIDS and Acquired Immune Deficiency Syndrome that's relevant to Scotland."

Because we were keen to attract people to the meeting.

Q. Yes. Are you able to say whether, from your own personal knowledge, there were any Glasgow patients at the meeting?

A. There were certainly quite a lot of patients I didn't -- or people I didn't recognise at the meeting and I assumed they had come from Glasgow or somewhere else in Scotland.

Q. Yes. I suppose they could have been spouses or relatives of your patients?

A. Some of them almost certainly were but people tended to sit together and if I recognised a man with a woman sitting next to him, I assumed that it was probably his wife. But there were quite a number of people there whom I didn't recognise -- who had come as pairs of people, if you like, I didn't recognise. So I think there were people from outwith the Edinburgh area.

Q. Yes. By a process of elimination you conclude that they were patients from outwith the Edinburgh area?

A. Yes.

Q. Did you have a meeting before the meeting with

Professor Forbes and Dr McClelland. Is that right?
A. That's correct, yes. No, I think it was -- we agreed -- I had agreed with Dr McClelland beforehand that he would come and talk about the blood transfusion aspects of it, a bit about our investigations of how we had -- how he had helped establish that this was probably, for the Edinburgh patients, a cohort, but not forgetting there were a number of patients who were positive in Edinburgh who weren't part of the cohort and there were obviously patients in Glasgow who were antibody positive.

So we certainly didn't gather beforehand and have a long discussion about the meeting. It was very informal. We agreed that Charles Forbes would open it and probably talk a bit about the background and the implications of the test and the consequences, and that I would talk about the cohort and Dr McClelland would talk about blood transfusion aspects and also to bring people up-to-date with how Blood Transfusion Service was trying to reduce the risk of further donations of -- blood donations that might have HTLV-III in them.
Q. Yes. Was it envisaged that there would be patients who had travelled from Inverness and Aberdeen at the meeting?
A. We thought it possible. I didn't hear on the grapevine that any were coming. That didn't concern me too much

because we didn't think that there were any individuals up there who were positive but I'm now just surmising, I'm sorry, I'm not sure.

Q. Yes, you said you heard on the grapevine. Does that mean that you phoned Dr Dawson back to find out if any patients were expected or ...?

A. I might well have sort of asked her did she have any patients that were coming. I'm sorry, I'm not certain about that. It's quite likely because I was keen to know what was -- that we get a good turnout.

Q. The news that had to be imparted, Professor Ludlam, was that some patients with haemophilia had tested positive for the new virus. Did you pass that news over to the meeting?

A. The information we wanted to put over was that their antibody test was positive, not that they were positive for the virus. I'm sorry to --

Q. You are quite right, I'm sorry.

A. -- nitpick but it is actually quite important.

Q. Yes.

A. I think Dr Forbes did that and I would have reiterated it. There was a certain amount of reiteration, is my recollection, in the meeting because it was all new for the people -- for the audience.

Q. Yes. Who, to the best of your recollection, spoke first

at the meeting?

A. I think Dr Forbes.

Q. Yes?

A. Because he was chairman and he introduced the meeting and I think -- my recollection is that he gave some of the background to HTLV-III and the testing and so on.

Q. Yes. He thinks you spoke first.

A. I'm pretty clear in my mind he was chairing the meeting. He was the senior physician. He "took charge" of the meeting, is my recollection.

Q. What did he tell the meeting?

A. I can't remember in detail but I think he talked about the test for -- the anti HTLV-III test had become available as a result of the virus, a probable virus that caused AIDS, being identified, and that samples had been tested from some patients and found to be positive.

Q. Yes. Did he just use those words "some patients"? He didn't distinguish between Glasgow or Edinburgh or anywhere else in Scotland?

A. I can't remember in detail. I think he would probably have talked about Glasgow and I would have talked about Edinburgh patients.

Q. Yes. So does that mean that he was telling the meeting that some patients had tested positive for the antibody test in Glasgow?

A. Well, I assume so because he must have had the information because it was published in the -- I think it was the Lancet three days later.
Q. Yes. The reason I'm asking, Professor Ludlam, is to try to understand whether the message was that some patients in Scotland have tested positive or that some patients in Glasgow and some patients in Edinburgh have tested positive?
A. I think it would be the latter. Some patients in Glasgow and some patients in Edinburgh, because I think probably patients in other parts of Scotland hadn't been tested.
Q. Yes. So that's what the meeting was told?
A. The former part of that, that Edinburgh and Glasgow patients had been tested. I'm not sure we would have said that patients in these other centres had not been tested.
Q. Yes, I see.
A. I'm just surmising. I'm not sure. I think it unlikely they would have been tested.
Q. Yes. Yes. So is that all that Professor Forbes talked about, the background, the fact that a test was available and the fact that some patients in Glasgow had tested positive? Was there anything else?
A. I think he would have explained what we knew about the

implications of being antibody positive. And at that stage the obvious question is: what's the chance of developing AIDS? And at that time we thought the risk was one in 500, one in 1,000, that sort of order, otherwise, unlikely.

Q. You say he would have. Can you not remember? Are you concluding that that is what he would have done?

A. I am because I don't remember.

Q. Yes.

A. But I'm sure, if you are going to talk about the antibody test to patients, then they are going to want to know what the implications of it are. So I'm sure that we will have talked about, as we understand it, the implications. Certainly that was one. The other one --

Q. I mean, I'm talking about Professor Forbes at the moment. I'm trying to just talk about what Professor Forbes told the meeting.

A. My recollection is that he dealt with the sort of generalities of anti HTLV-III testing and positivity, and obviously the other thing is the implications that people -- that people with haemophilia may have the virus even if their antibody test is negative and that, as was known at that stage, it was sexually transmissible.

Q. Yes.

A. And one of the important messages we were keen to get across at the meeting was that patients' sexual partners would be at risk and that patients should use condoms during sexual intercourse.
Q. Did Professor Forbes address that issue?
A. I think it likely. I know it was well discussed at the meeting.
Q. Yes. Who spoke next, Professor Ludlam?
A. I suspect probably me.
Q. Yes.
A. To explain what had been happening in Edinburgh, what I had been doing, what the results of the tests were.
Q. When you say "what I had been doing"?
A. Sending the samples to Dr Tedder.
Q. Yes.
A. And that it appeared that there had been this single batch of Factor VIII, but also there were other people who were or might be infected or might be antibody positive.
Q. Yes.
A. It was a time of great uncertainty and we were very careful also to convey the message that if you were antibody negative, you weren't necessarily free of HTLV-III infection, and so the advice was for everybody to consider they might be infectious, everyone with

haemophilia might be infectious, and it applied -- the advice, the safety advice applied not only to the possibility of sexual transmission but if there was spillage of blood, it should be cleaned up carefully with gloves on and using dilute bleach to sterilise the surface.

Q. Yes. Is there anything else that you told the meeting?

A. Well, we --

Q. I'm specifically asking what you remember about what you said, Professor Ludlam.

A. Yes. There was -- the very clear message given out was that we hoped that patients would come and see us and ask about their situation. We were keen to discuss it with people individually. That was not just the people who were HIV positive. They didn't know who they were. We were keen to see everybody.

Q. Is that how you put it, that you hoped that patients would come and see you about their situation?

A. We would have encouraged them to, yes.

Q. Sorry, we are at cross purposes. Is that how you would have put it? Are those the words that you would have used to the audience, that you hoped that patients would come and see you to discuss their situation?

A. And to learn the results of their test.

Q. Yes. Well --

A. Although that is actually of lesser importance than coming to discuss their situation.
Q. Yes. Well, that's another matter but are you saying that as well as saying that you hoped patients would come and see you about their situation, you also said that patients -- I don't want to put words into your mouth. What did you say about testing, if anything?
A. If they came to see me, if I had the test result from Dr Tedder, and if they wished to know it, then I would let them have it. But I would also want to suggest that they give another blood sample to, if you like, confirm the preliminary result from Dr Tedder, both because of the possibility of samples being misidentified or false positives or false negatives in Dr Tedder's test.
Q. Yes.
A. And I would have talked round the importance of the possibility they might be infected even if they were antibody negative.
Q. So you said something like: if you had the results, you would let them have it. Something like that you said?
A. I would give them the result, if they wanted to know it.
Q. Yes. So you have a recollection of giving that message to the meeting?
A. Yes.
Q. Sir, I think that for --

THE CHAIRMAN: Yes. I think we have got to stop at that point.

See you on Tuesday, professor.

(4.02 pm)

(The Inquiry adjourned until Tuesday, 21 June 2011 at 9.30 am)

I N D E X