Wednesday, 18 May 2011

(9.30 am)

PROFESSOR ANDREW LEVER (continued)

THE CHAIRMAN: Good morning.

MS DUNLOP: I think the point we have reached, sir, is that it's the turn of those in the front row to ask such questions as they want to ask.

THE CHAIRMAN: That was the position last night but I never retain the confidence that it will be maintained overnight.

Mr Di Rollo?

MR DI ROLLO: Mr Dawson is going to ask the questions.

Questions by MR DAWSON

MR DAWSON: Good morning, professor. Could I start by asking you a few questions about a period you were asked about yesterday. That would be the spring of 1983. Could we have up on the screen, please, a document which you weren't taken to yesterday but you did discuss. That's [DHF0014474].

This is the document to which reference was made yesterday, namely the Haemophilia Society letter of 4 May 1983 incorporating some advice from Professor Bloom. I think you are familiar with this letter. Is that right, professor?

A. I am, yes.

Q. And you will see in the main block that there is an opinion expressed by Professor Bloom to the effect that AIDS has not yet been proven to result from transmission of a specific infective agent in blood products. You spoke yesterday about the requirement that people should be reassured in the context of this letter.

If you had been asked in May 1983 for your view as to the aetiology of AIDS and the risks of contracting it from blood or blood products without the burden of having to reassure your audience, how would you have expressed yourself?

A. I think it's difficult to separate the two entirely, if I might say, in that giving completely unguarded advice without considering the impact that it might have isn't something I think I would want to do. So I think in this and other circumstances you could argue that it would be, not exactly reckless but inconsiderate to be giving advice without considering the consequences.

I think my wording would have been not dissimilar to Professor Bloom's, in that it was not proven. I think if I were speaking to an audience in whom it was not the case that I was trying to reassure, I would have probably implied that I thought it was quite likely that it was an infectious agent transmitted by blood products.

Q. Thank you. What pieces of evidence would particularly have influenced your view at that time?

A. I think the knowledge that there had been retroviruses already implicated in human disease in the form of HTLV-I and that that particular virus was known to target a cell population in the blood called the lymphocytes, and that there was evidence in this illness that there was dysfunction of the lymphocytes and the epidemiology, which has been visited quite extensively so far, of the fact that there appeared to be clusters in particular geographic areas and, of course, the fact that sexual transmission of infectious diseases is extremely well documented, as indeed is blood transmission of infectious diseases.

Q. I would like to come back to this document but could I just jump for the moment to your statement, in particular page 5. The statement is [PEN0150517]. In the paragraph which starts with, I think, a reference to the preliminary report, 8.25, you discuss this letter, and you say there that:

"Whilst true ..."

That's the comment to which I have just made reference:

"... appears to ignore much circumstantial evidence."

Then you say:

"... and consensus opinion in the majority of doctors that a transmissible agent, almost certainly a virus, is the most likely aetiology."

I just wanted to flesh out a little bit who you were talking about when you said "the majority of doctors". Would that include haemophilia doctors and transfusionists to your knowledge?

A. I think one's opinion is always coloured by the people one works with and certainly I work with infectious diseases people and have done for many years, and I think that may in part reflect the people I work with, and I would hesitate before assuming I knew what the haemophilia doctor population were thinking at the time.

But I think in discussion most doctors that I came into contact with and much of the published literature at the time as well, including articles in the Lancet, had suggested that a transmissible agent, which was blood-borne, seemed a very likely candidate. So I think that may be a consensus of many doctors in different disciplines but not every doctor in individual disciplines.

Q. I understand. From what you have just told us there, would it be fair to say that the consensus opinion was not only as you say there, that a transmissible agent,

almost certainly a virus, is the most likely aetiology, but also that the virus could be blood-borne?

A. Yes.

Q. Thank you. While we are on that page, I just wanted to ask you about a comment that you make in the top paragraph of that page. You say in the final sentence there, under a reference to the period March 1983, so slightly before the letter we have been looking at:

"The connection between AIDS and blood products, particularly commercial blood products, from the US appears to be very strong."

I just wanted to ask you: in that sentence, is that you expressing your opinion of the state of affairs at that time or is that you referring, as I think you do throughout this passage, to what's contained within the preliminary report?

A. That's a reference.

Q. To the preliminary report?

A. Yes.

Q. Yes. Does that represent your view on that matter as at that time?

A. I think there was a general knowledge that the sourcing of donations for blood products in the UK and in the United States was very different and that it was known that paid donors as a whole were more likely to carry

infections. So I would say that would reflect my opinion as well.

Q. Thank you. If we could just go back to the Haemophilia Society letter, please, [DHF0014474], you will see, professor, that shortly after the sentence to which I have made reference starting "The cause of AIDS", the passage from Professor Bloom places some reliance on the fact that neither have any cases been reported from Germany, where massive amounts of American concentrates have been used for many years.

Can you be of assistance to us as regards the accuracy of the reference to Germany at that time, both from the point of view of the usage in Germany of American concentrates and also whether at that time there had been any cases of AIDS in the German haemophiliac population?

A. I have no information about the usage of concentrates in Germany. Similarly, I don't know any facts about the reported instance of immunodeficiency in the German population either. There was, I think, still at that time a lack of perception of cases which were developing into AIDS as I implied in my report. There may have been cases which were not recognised as such but that is speculation.

Q. Thank you. Had Professor Bloom chosen to look to other

countries in Europe at that time for examples of the extent to which there had been infection or suspected infection amongst the haemophiliac population, other than Germany, what information might he have found?

A. Again, I don't have information on the perceived or actual detection of AIDS cases in other European countries other than the few comments I have made in my report of Denmark and the single case in Italy.

Q. Thank you. It's true to say that there is no reference there to the question of how many haemophiliacs were infected at that time in the United States. Can you be of assistance just in pinpointing what the statistics might have shown at this point in time, had such a reference been made?

A. Is the question, had we had a test for HIV at the time?

Q. What the information was that was available at that time as regards possible infection amongst the haemophiliac population in the United States.

A. I would have to refer to the documents that have been quoted in the report to give you numbers because I am afraid I don't carry those in my head.

Q. I have got no difficulty with that at all.

A. It may take a moment or two.

Q. Thank you. (Pause)

A. It may be helpful if I have a hard copy of the report to

look at as well.

THE CHAIRMAN: What do you want to refer the professor to, Mr Dawson? I don't think it's fair to send him simply on a search through the documents. Do you have a specific date, the date of the letter? What are the source documents that you think you might like him to look at?

MR DAWSON: I don't have any particular source documents in mind.

THE CHAIRMAN: Mr Dawson, it is up to you to have them.

MR DAWSON: I understand that. I'll move on from that question, sir.

THE CHAIRMAN: As far as you are concerned, professor, do you have any concern about the accuracy of the references in the report, since you have read it, giving data at or about the time of this letter?

A. I don't have any concern with those.

THE CHAIRMAN: Well, Mr Dawson, unless you can point otherwise, we will simply take the report as it is.

MR DAWSON: Indeed, I'm obliged.

Could I ask you just one final question about this letter. There is a reference in the final sentence here to certain experts. It says:

"We should avoid precipitate action and give those experts who are responsible a chance continually to

assess the situation."

Can you be of assistance to us as regards who those experts who are responsible might have been in Professor Bloom's mind at that time?

A. Professor Bloom would have wanted as much information of an epidemiological nature as possible from as many countries as possible, as were using concentrates, and the sorts of sources of information would have been the MMWR reports and the CDSC reports.

Without good statistical information about the development of what turned out to be an epidemic, one would have trouble predicting it but those were the primary sources that he would be hoping to get it from. In addition, he would also be wanting information from people who were striving to actually isolate an infectious agent.

Q. So --

A. Scientists and virologists.

Q. So virologists would be amongst those who would be responsible for looking into the situation at that time?

A. They would be beginning to be involved at that stage, yes.

Q. Who in particular would have been involved in the virological community?

A. There are at that time not many people actually in the

world who are very much experts in retroviruses but there were quite a lot of people who were experts in virology, some of whom are named here. So people like Dr Tedder, for example, people who had connections with the Blood Transfusion Service from investigation of other viruses and those who investigated hepatitis viruses, for example.

Q. Do you think it would be fair to sum up the content of Professor Bloom's message as saying that at this stage we don't really know what the position is, so we should just continue as regards the use of blood products as we have before?

A. I think in fairness he is not ignoring the issue; he is saying that there is something we have to keep an eye on but at the moment we don't have enough information to inform action which we can confidently say is the correct way forward.

Q. Indeed. Thank you. You were referred yesterday to the views expressed at almost exactly the same time as this by Dr Galbraith and you gave us some explanation of that. Could we have up a document, please, [MIS0010001]? This wasn't a document you were taken to yesterday but was a subject matter upon which you made some comment. Is this a document that you are familiar with?

A. I am, yes.
Q. It is a letter, which although it is not entirely clear, I have gleaned from the preliminary report is dated 9 May 1983, so five days after the document that we have just been looking at. In this document, Dr Galbraith in a letter to Dr Ian Field says:

"I have reviewed the literature and come to the conclusion that all blood products made from blood donated in the USA after 1978 should be withdrawn from use until the risk of AIDS transmission by these products has been clarified."

I would just be interested to know your comment on the apparent difference between the position being taken by Professor Bloom and the position being taken by Dr Galbraith, both of which appear to be based on a lack of complete understanding of the position, but one of which appears to suggest continuing with the position as it was, and the other suggests that in light of the lack of complete understanding, something needed to be done.
A. Yes. They completely come from a very different background.
Q. Of course.
A. Dr Galbraith is looking at this entirely from an infection point of view, without, in many ways, considering the consequences of doing this and to some

extent doing perhaps what you requested I did, which was to give advice without necessarily thinking through all of the implications of it.

So from a purely objective point of view, if he feels that there is sufficient information to suggest that there is an infectious risk, his duty as the person that is acting in the public interest from an infectious disease point of view, is to apply a precautionary principle and say this is what one should do.

I don't disagree with his comments in terms of the likelihood of there being an infectious cause and an infectious risk. I suspect the difference between him and Professor Bloom is that he doesn't perceive what has happened to the haemophilia population over the previous 20 or 30 years, the benefits of blood products, and the change in their lifestyle that this sort of action would incur and also the fact that nobody at that stage knew whether this was going to be a rather short-lived, relatively unexciting, epidemic, such as the SARS epidemic which burned out very rapidly and doesn't seem to have come back, or whether it was going to turn into something which was extremely tragic, as it did.

Q. It does appear that the position as regards the haemophiliac population in the United Kingdom is certainly something which Dr Galbraith is taking into

consideration here, in particular in the first sentence he says:

"Last week whilst you were away in Geneva, a case of the Acquired Immune Deficiency Syndrome in a haemophiliac in Cardiff who had received USA Factor VIII concentrate was reported."

So that would date it as before either of the letters we have looked at, the other one being five days before this. I think you were asked some questions about that case yesterday. But I would just like to see if you could give us a bit more information as to how well-known at that time the infection or the reports of infection in the haemophiliac in Cardiff actually were?

A. In the infectious disease field and certainly in the microbiological field, the CDSC reports, which were regularly issued, were generally looked at. So the infectious disease community would have been aware of it, other specialities probably not. The haemophilia doctors' community, I suspect, would have been but not necessarily from the CDSC report because that must have been reported after the actual event.

Q. Okay, thank you.

THE CHAIRMAN: Mr Dawson, could I go back just a little and pick up a point that you made?

MR DAWSON: Of course.

THE CHAIRMAN: You have indicated that in May 1983 Dr Galbraith would have been required to follow a precautionary approach. Was the precautionary principle well established at this time in the way it came to be established by the early to mid 2000s?

A. Dr Galbraith does not know what's going to happen when he says this. There is no doubt about it, and I think he is being very cautious, which is an understandable position from his point of view, in that if his position is to warn the population of risks of infection, then it's his duty to do so as early as possible and to be relatively unequivocal about it, rather than to imply that there is a new infection and we don't really have to worry. But he does not know the unfolding of the epidemic as it occurred.

THE CHAIRMAN: But his duty would derive from the particular nature of his office.

A. Exactly.

THE CHAIRMAN: And the obligations that went with it?

A. Very much so.

THE CHAIRMAN: Does that imply that from his point of view a balance would be less important as between the possibility of an emerging risk and the benefits that might attend it?

A. I think everyone is coloured by their own particular

perspectives. So his perception of an infectious risk would be dominant in his mind as he thought this through. And more so than the consequences to the population that he would be influencing, were his words to be translated into actions.

THE CHAIRMAN: I'm anxious, Mr Dawson, that we don't get the balance wrong and I don't think I fully appreciate the point of view that would be held by each and every specialist around this time. But if you want to follow this and tighten up on just exactly what Dr Galbraith's office would have required him to do, it might help.

MR DAWSON: Indeed. What I intended to move on to was a slight refinement of this position, which was to ask about the contact between the different specialities.

THE CHAIRMAN: That might be fine.

MR DAWSON: You gave some very interesting evidence yesterday about the history of infectious diseases as a medical speciality, if you like, and its recognition varying over the history.

To what extent was virology a recognised medical speciality at this time, in the early 1980s?

A. Virology is and always has been part of clinical microbiology but it was certainly an independent discipline within clinical microbiology. So there would be consultant virologists at all of the larger hospitals

and there would be access to virological expertise in all hospitals. So virology was in the health service certainly an established discipline, and of course outside of that there was and is a very large amount of basic research going on in virology.

Q. I think you touched on this, but at that time how easy would it have been if a haemophilia doctor or a transfusionist wished to seek the opinion of a virologist on these important matters? How easy would it have been for such doctors to do so?

A. I don't perceive there would have been significant difficulty at all.

Q. You referred yesterday to the development, I think, in the aftermath of the HIV outbreak of the development of multidisciplinary teams and my understanding of your evidence was that you thought that they were rare at this time but they had developed subsequently and that their advent was something to be welcomed.

Even if the support of a virologist had been available, do you think at that time that it would be likely that a haemophilia doctor would have sought out the opinion of a virologist on these matters?

A. Yes, in answer to your first point, just to clarify, I think probably multidisciplinary teamworking started with the cancer world, which was the major driver behind

that. I don't think it would have been difficult or unreasonable for somebody in the haemophilia field to be discussing this with a virologist. Virological expertise at the time was still relatively rudimentary. I don't mean to insult my colleagues from the time but there were a limited number of viruses that one could grow in culture in the laboratory and it was a common observation that virologists tended to give you a result long after the person had either got better or not.

That was partly because the viruses are difficult to isolate and they are difficult to grow. They are very fussy. And partly because a lot of diagnoses were done in retrospect by detecting antibodies against the virus that had been there. So quite commonly it was a post hoc diagnosis.

However, for infections such as Hepatitis B, then involvement with virological laboratories was very close in fact. So chronic viral infections did involve a large amount of interaction between, for example, doctors looking after patients with liver disease and the virological community, doctors looking after patients who were having transplantation, who were immuno-suppressed and were prone to viral infections, and certainly, as far as I'm aware, doctors who were looking after patients with haemophilia would consult

with virologists in the diagnostic laboratory at regular intervals.

Q. Thank you. One of the haemophilia doctors from whom we have heard evidence in this section told us in his evidence, in the context of there requiring at a later stage to be a designated physician in each area for AIDS, that in his area he seemed to be the only doctor who knew anything of AIDS and therefore they suggested that he should be the nominated AIDS physician.

It seems to me that that paints a picture of there being little local expertise. Perhaps there might have been some difficulty seeking out and receiving the opinion of a virologist, even if one felt that way inclined as a haemophilia doctor.

Do you think that that paints an accurate general picture or do you think that may be just a local exception to the general rule?

A. I think you have to distinguish between laboratory virology and clinical infectious disease expertise. Most laboratory virologists would work in the laboratory doing diagnostic work and would rarely if ever, venture onto the wards and consult with patients or see illness in the round. They would be dealing with specimens rather than people. To some extent that's still the case; to a large extent that's still the case.

Then laboratory virologists were very much the norm. They would be consulted but would not necessarily involve themselves in management of infections to that extent. Clinical infectious disease expertise, as I expressed before, was relatively patchy and there were relatively few, compared to other disciplines, infectious disease physicians, and at this stage, of course, there was almost no expertise at all in the UK on HIV/AIDS amongst clinicians and that was reflected over the following five or ten years by the fact that in, not the minority but in the small majority of hospitals which did have some sort of infectious disease expertise, which tended to be large teaching hospitals, the infectious disease physicians did get involved in managing patients with HIV/AIDS. But in many hospitals up and down the country, it was what is termed an organ-based specialist who became involved. So people who were gastroenterologists or respiratory physicians, who took an interest in these particular things.

I think you have had Professor Gazzard here. He is a gastroenterologist originally. But there wasn't an infectious disease physician in his hospital so he became interested in AIDS and took it on and became a world expert on it. In other hospitals it was the local respiratory physician who became interested

because of pneumocystis, and took it on.

So there was a relative lack of clinical infectious disease expertise. There was access to laboratory virological expertise but these were not people who would be involved usually in the management of patients directly.

Q. Do you think that at this time an infectious diseases expert would be better placed to form a view on the risks of AIDS, and in particular the risks of transmission of HIV by blood products given perhaps greater understanding of the topic, perhaps greater access to materials, and given the fact that as you said, such experts, unlike haemophilia doctors, would be unburdened by the types of considerations that you mentioned as being in the mind of a haemophilia doctor at this time?

A. I don't believe that infectious disease doctors are all powerful and vastly superior in their skills to other physicians. I can perhaps quote one of my colleagues, just to reflect this, and this is somebody who was a haemophilia doctor at the time. He pointed out that their understanding of infection was such that, when they saw patients who were developing AIDS or patients with haemophilia had antibodies, they thought everything was okay and there wasn't a common perception that you

could have antibodies and still not be okay, because they didn't have the breadth of exposure to patients with other infectious diseases.

So it would be reasonable to say that an infectious disease physician would have a broader perspective and perhaps a deeper understanding of an infection. Even so, at the time this was such a new and such an unusual, and as I have said before, such a unique infectious disease phenomenon, that I don't believe anybody would have predicted accurately what actually happened.

Q. Sir, I was going to move on from that topic to another topic now.

Would it be correct to say, professor, that at the beginning of the 1980s it was known that the use of blood products would involve transmission of certain viruses?

A. It was known that there was a risk of transmission of viruses with blood products, yes.

Q. What viruses at the beginning of the 1980s would there have been a risk of transmitting through blood products?

A. Hepatitis B was well established and at that stage the other hepatitis viruses had not been classified. So they were called non-A non-B but there was already epidemiological evidence that there was more than one non-A non-B virus because people had documented more

than one episode of acute hepatitis and jaundice in transfusion recipients in the past, but the exact numbers of agents was not known, nor were they characterised.

Q. Right. Are there any other viruses that would have been on the mind of clinicians at that time?

A. That's a good question. Somewhere around that time -- and my memory fails me -- I think parvovirus was identified as being in blood products or in blood.

Q. If it might be of assistance, professor, I have something particular in mind here. This isn't from the beginning of the 1980s, and I did ask the question about the beginning of the 1980s. This is something from an article to which the Inquiry has had reference, by Barbara and Tedder from 1984. There is a list there of viruses which are deemed to be transmitted by blood and its blood products.

Perhaps it might be useful to have that up. It's [LIT0013739]. We are looking at the second page of that document, which is LIT0013740.

Just to be very clear, this is an article which is written in October 1984. My question is directed to earlier than that, ie to the beginning of the 1980s, but there is a list there in table 1 of viruses transmitted by blood or its products and you mentioned some of

those. Hepatitis A, Hepatitis B and delta agent, non-A non-B hepatitis, parvovirus, cytomegalovirus, Epstein Barr virus and HTLV-I, to which you made reference yesterday.

A. Yes.

Q. This is obviously from a different time but these were the types of viruses that I was wondering about and whether there will be a known risk of transmission of these viruses at the beginning of the 1980s.

A. So there is a slight nuance here in that Hepatitis B, non-A non-B and HTLV are normally transmitted by blood, in that that is their route of transmission. Cytomegalovirus, Epstein Barr virus, if they are present in blood, are, but that's not their normal route of transmission. I perhaps misinterpreted your question as to what can or what is usually in the natural course of events.

Hepatitis A is, as it says, rarely; that is transmitted by the faecal/oral route. It's an orally acquired agent. Parvovirus. I confess to not knowing a great deal about parvovirus transmission because it is not clinically very important, apart from in patients with sickle disease in whom it causes a red cell aplasia. So I presume that says it's in the blood and then therefore can be transmitted by blood products, but

I don't again believe that's its natural route of transmission.

Q. Right. Okay. What I'm thinking about in particular was some evidence you gave yesterday about the risk/benefit analysis of administering blood products but which I understood you to mean the balancing of, first of all, the risk of viral transmission, as against the clinical benefits of using certain products. Is that a correct interpretation of what you describe as the risk/benefit analysis yesterday?

A. Yes.

Q. As I understood your position, you were of the view that at the start of the 1980s, the position was that despite the risk of certain of these viruses possibly being transmitted by blood, the general consensus was that the risks of viral transmission were outweighed by the benefit of treatment. Is that right?

A. Yes, and I can run through that list and point out why, if you like.

Q. Well, I'm less interested in knowing particularly why but what I'm interesting in knowing is what happened when HIV came along against that background. First of all, could I just clarify that it would be correct to say, would it not, that from its earliest manifestations, one of the defining characteristics of

AIDS was the suppression of the immune system? Is that right?

A. So the earliest characteristic was evidence that the lymphocyte populations were affected. That was the earliest sign before people developed overt disease. But the disease manifestation is exactly that: it's evidence of a suppression of the immune system or depletion of the immune system.

Q. And I think you referred yesterday to opportunistic infections.

A. Yes.

Q. Which I understood to mean infections which would be more likely to cause difficulties for patients with a suppressed immune system than they would in a healthy patient?

A. That's correct, yes.

Q. In light of the threat of an immuno-suppressant virus, do you think that there required to be a reassessment of the risk/benefit analysis in light of the risks of the transmission of various viruses at the time when HIV came along?

A. It becomes another exercise of retrospective view.

Q. Of course.

A. Because risk/benefit is a combination of risk/benefit to individuals and to the population as a whole. Whereas

all of the viruses that had been mentioned here in your previous list are ones in which it was established that the benefit from the treatment far outweighed the risk. It's now clear, very clear looking back from this perspective, that the risk/benefit was against the continuing use of blood products if they were transmitting HIV.

I think there probably was a reassessment in people's minds as to whether or not this was going to be more serious, as there would have to be because there had been deaths. But there was still no knowledge of whether this was going to be an isolated, small number of deaths amongst a very large majority of people who had no disease whatsoever. The difficulty that the physicians at the time were in was the fact that the virus takes so many years to manifest itself through its incubation period to producing full-blown disease. But I think your statement is correct in that if there is evidence of immuno-suppression and there is evidence of death from immuno-suppression, it should, and I'm sure did, trigger a reassessment of risk/benefit.

Q. Thank you very much.

Could I just ask you, in relation to the evidence you gave yesterday, about the various theories related to AIDS in the early days? In particular I want to ask

you about a comment that you made on page 3 of your report. Could we have that up, please? That's back to [PEN0150517] at page 3. I'm looking at the very bottom paragraph of that page.

This is the section, professor, in which you have just started your analysis of the emergence of AIDS and you are telling us about the information or the evidence that was available and the theories that were starting to spring up. You say there:

"There was speculation at the time ..."

This is in the early days in the middle of 1981:

"... that cytomegalovirus or Hepatitis B, possibly a new, more virulent strain of one or the other, might be responsible for this disease as all of the individuals were positive on testing for both of these viruses."

Is there an explanation as to why the individuals who were exhibiting the signs of HIV were also positive for these other viruses, with the benefit of hindsight?

A. The homosexual population?

Q. I think you are talking here about people who are exhibiting signs of HIV infection, and a theory sprung up that it might be something to do with these two viruses as all the people had tested positive for these two. I just wanted to know whether there was an

explanation as to why it was that they were positive for these viruses as well.

A. Well, both can be sexually transmitted and this was a very sexually promiscuous population.

Q. You were also asked yesterday and gave evidence on what was described as the antigen overload theory. Could you just explain for me at what point in your chronology the antigen overload theory, on a balance of probabilities, become not the most likely explanation as to the aetiology of the virus in haemophiliacs, if indeed it ever was judged by that standard to be the most likely explanation?

A. Yes.

THE CHAIRMAN: I think the double-headed hypothesis here is a bit difficult. Perhaps we should unpack it just a bit.

I think that I know, from Professor Ludlam's publications, the sort of period over which his particular subjects were studied and found to be immune-suppressed, and that might give us a timeframe for one aspect of it, Mr Dawson, unless you can take it further back.

MR DAWSON: Perhaps an easier way of putting it would be first of all to say: was the most prevalent theory the antigen overload theory at any stage over this period?

A. I think it was a competing theory. It's difficult to give statistics but one might remember that the antigen overload theory probably originated in New York amongst the physicians looking after patients with HIV and amongst the gay population in New York themselves, because they felt that if it was perceived that there was an infectious cause -- this is again hindsight -- that the gay population might be more stigmatised for transmitting agents which caused disease.

I think the first reference goes back to a physician, whose name escapes me, in New York, putting this forward as an alternative, less stigmatising theory. The stigma is very real and occurred right the way through in the Montreal conference. There was a series of unprecedented takeovers of the stage by different pressure groups protesting about what had been seen to be media perceptions or medical profession perceptions. I remember the prostitute population taking over the stage and complaining very much that being referred to as vectors of disease was a very demeaning thing.

So that's, I think, where it came from and would have established itself in a lot of people's minds who had vested interests in there not being a virus, similarly to, I think, the phenomenon in South Africa,

where it was deemed to be politically better for there not to have been a virus produced in Africa which caused the infection. That carried on, as you know, until very recently.

Q. One could have asked oneself the question at any stage in this chronology: on a balance of probabilities, which is the most likely to be accurate of all these theories? Was there any point at which this competing antigen overload theory would have been the most likely?

A. I don't think at any stage it was the most likely. I think it was competitive but I don't think at any stage it was the most likely. Largely because it was based on a speculation as to the effect of protein overload, for which there wasn't precedent.

Q. I think you gave some evidence about that yesterday. Is there a point in the chronology where the antigen overload theory becomes no longer sustainable?

A. To my mind, when the virus is isolated.

Q. But not at any stage earlier than that?

A. I think, as I mentioned yesterday, there is a gradation in belief that some people will have been very convinced after the Montagnier/Barre-Sinoussi isolation, others wouldn't. Others, particularly Americans, would have been convinced after the Gallo. So there would have been a slow change.

Q. So the point at which the antigen overload theory would have been put to one side would depend on how convinced one was about the discovery at those two different points?

A. Very much from ones own personal perspective and where one lived and worked, yes.

Q. You talk at length in your statement about something which I have referred to already, which is the balancing exercise which requires to be carried out in haemophilia care between the risks of products and the benefits of products. I just want to ask you about one of the things that you say on page 5 of your statement, so two pages from where we are at the moment. Looking at the second bottom paragraph. I'm looking at line 7 of that. A sentence which begins:

"To maintain ..."

Do you have that, professor? It's the second bottom paragraph, line 7 of that. There is a sentence beginning:

"To maintain ...

A. Yes.

Q. It says there:

"To maintain the factor concentrate availabilities, the directors knew that they had no option but to continue to source blood products from the USA."

This is in the context of you discussing, I think, what I have described as the balancing exercise and pointing out your understanding of the considerations on one side and the considerations the other, as to whether to continue to use certain products. I just wanted to ask you what the source of that comment was about continuing to source blood products from the USA?

A. This was my impression from the documentation that I received with the preliminary report.

Q. Right, okay. Was that comment then made with the United Kingdom in mind or Scotland in mind?

A. Both.

Q. Okay, thank you.

I would just like to jump back now to something which you were mentioning earlier and this is another component, I think, in what I have described as the balancing exercise, but this is one of the factors that you have brought out. One of the things that you refer to -- and I think this is probably best described at the top of the next page, on page 6. Perhaps it would be easier just to go to that and read out the second paragraph. Again in the context of this balancing exercise:

"Although AIDS itself clearly had a very bad prognosis, there had not been enough longitudinal data

to say what percentage of individuals, who were infected with the putative agent, actually went on to get the disease. It might, as with some diseases, for example HTLV-I, be a very small percentage who became ill and the risk/benefit ratio of being infected versus not receiving clotting factor concentrates was not clearcut".

I think you have mentioned this already this morning. I think there you are talking about two different considerations. One is the number of people who might go on after infection to become ill and that was the thing that wasn't known at that time. Is that correct? That's the first thing?

A. That's true.

Q. The second thing you are talking about there is for those who do become ill, that there was -- and it was known at that time -- a very bad prognosis?

A. That's true.

Q. Those are two separate considerations in this balancing exercise. Is that correct?

A. They are both part of a balancing exercise but they are separate considerations, yes.

Q. Thank you very much. I just wanted to ask you a couple more things. The first was something that I think you talked about yesterday. I just want to be clear that my

understanding of it is correct. One of the other witnesses who has given evidence in this section in the context of talking about transmission of HIV via blood products used the expression "viral load". What's your understanding of that expression?

A. It's a mathematical estimation of the number of viruses per unit volume of the plasma. And we use it clinically to judge whether or not a person has early or advanced disease and also the success of antiviral therapy. The methodology is an amplification technique, but one effectively counts the number of viruses or the number of genomes of the virus, the number of pieces of RNA of the virus in a unit of blood, usually 1 millilitre. So that somebody who is uninfected is zero. In somebody who is very well treated it is less than 50 because that's the limit of detection of the assay. People who are unwell may have many thousands or many million copies of the virus per ml of blood.

Q. I'll move on from that topic. The final thing I wanted to ask you was at what point in the chronology did it become known that HIV could be sexually transmitted? I think yesterday in the context of the correspondence between Dr Craske and Dr Ludlam you made some reference in connection to the fact that there had been some studies done amongst the haemophiliac population, which

were of assistance in reaching the conclusion that HIV could be sexually transmitted. I was just interested in knowing what it was you had in mind and whether that was in fact the point in time when sexual transmission became accepted?

A. No, sexual transmission was believed to be the case from very early on, both in terms of homosexual transmission as clearly a risk factor but also evidence of infection in the heterosexual population.

It's actually a very good and difficult question to answer as to when it was absolutely certainly known that a virus was transmissible from one person to another and that probably occurred in the late 1980s. I can remember the paper because it was in Science, but I can't remember the exact date when the virus was isolated from somebody who was newly infected and shown to be, with the techniques that were then available, identical to the virus from the person who they appeared to have acquired the virus from.

Q. Was that when it definitely became --

A. That's when you could not deny there was any other way that it had been transmitted. But, as for many virus infections, the epidemiology is often as indicative. So, for example, if you look at the antibodies in people to a virus like herpes simplex type 2, which is HSV-2,

genital herpes, then they are very uncommon in people under the age of 12. And if you look at the population as a whole, then the percentage of people with antibodies to herpes type 2 rises in the late teens. So the implication there is that sexual transmission is occurring.

In fact I don't think any virus has been as accurately analysed as HIV. I don't think anybody has actually taken a herpes simplex type 2 from a donor and compared it to herpes simplex type 2 from a recipient and said they are the same virus. So all of the evidence of sexual transmission comes from the epidemiology.

Q. The reference that I picked up yesterday about there being a study amongst haemophiliacs in this regard, what was that about?

A. Again I would have to refer back to the report but there was a case of a spouse of a haemophiliac becoming infected.

Q. You have described the point at which it became certainly known that the virus could be transmitted sexually. The documentation we looked at yesterday, I am thinking of this letter from Dr Craske to Dr Ludlam, was more in the mid 1980s, and there was reference there to Dr Craske's understanding at that

point that the virus could be sexually transmitted. Of course, we went through that list and some of the things were right and some of the things were wrong, but that was one of the things that you had said was correct. At what point was it the prevalent view that sexual transmission was a possibility with HIV?

A. I think from the word go actually. It was believed it was sexually transmitted.

Q. Thank you very much, Professor, thank you.

Sir, I have no further questions.

THE CHAIRMAN: Professor Lever, I'm going to have to come back to the very early stages of the development of the antigenic overload theory and it may be there is some literature that I will have to have Professor James dig out for me to make sure that I understand it, but is it right to understand the position generally to be that after a reasonably significant number of cases of AIDS in homosexual men had been recorded, there was an extensive study in New York of a large number of homosexual men and in particular a study of their immune indicators? Is that a starting point?

A. Yes, and my memory for the literature isn't perfect either. As I recall, there was evidence of immune dysfunction but also the presence of anti-sperm antibodies, indicating perhaps that there had been

exposure to proteins which the immune system wouldn't necessarily normally have encountered.

THE CHAIRMAN: So leave the anti-sperm antibodies aside just for the moment. One element that did emerge was depression of the T4:T8 ratios right across a broad spectrum of homosexual men. Out of that did the theory develop that it might be a progressive sort of condition, as it were, leading to immuno-suppression in this population that might not be associated with an infective agent but with the accumulation of exposure to things like sperm and other factors? How does one explain it?

A. I'm not a career immunologist. So I would have to give you my understanding of this but you can influence lymphocyte populations, you can manipulate the immune system in rather specific ways, as I mentioned before, by things like desensitising procedures. One could construct an argument that abnormal exposure to proteins would do something but the details of it, I think, would be very difficult to tease out and be very specific about and say this had a precedent that would specifically do what happened to the lymphocyte cell populations. I'm sorry, that's not a very satisfactory answer.

THE CHAIRMAN: Not very satisfactory. I don't need all the

answers at the moment and perhaps --

PROFESSOR JAMES: I mean, my understanding is that they were obviously faced with the first 20 or 30 AIDS cases, let's say, in a population of gay men in New York, casting around for the first beginning of ideas as to the possible cause. They screened a pretty large number of gay men and I think one of the studies is in the New England Journal but I'm going to check these references for the Inquiry.

Among other things but principally they found this suppression of T4:T8 ratios in otherwise well individuals and then obviously it was a matter of, if you like, casting around for theories which might explain this. One of the theories that was put forward, in a rather inchoate fashion but perhaps with greater immunological expertise, certainly greater immunological expertise than I have, even then, was that it could be due to antigen overload as witnessed by the presence of anti-sperm antibodies and so on. I believe that in those papers obviously they also mentioned, well, this could be an infectious agent, we just don't know but that's my understanding of how that theory originated pretty early on in the game.

I mean, we will check on that but would that fit with your understanding as well or is that not correct?

A. No, it's correct but it also reflects what I said yesterday, that the initial manifestations of HIV don't look like a normal infection.

PROFESSOR JAMES: Yes.

A. They look like something is leading to a degeneration or a deterioration in the immune system and there hadn't been another infection which clearly did that, and that's why not only theories of protein overload but theories of specific drug abuse like amyl nitrate were brought up because it could be a toxic effect in the immune system, and all of those were as plausible as each other. I don't think any one of them had a majority view at the very beginning.

THE CHAIRMAN: To bring in Professor Ludlam's work here, he in effect did the same sort of screening of a large number of haemophilia patients and found a pattern of suppression that seemed at least to have some parallels with that that had been reported from New York. Is that a correct understanding?

A. That's correct. Again, in the absence of an illness that looked like conventional infection, one would look around for competing theories.

THE CHAIRMAN: I think it is going to be quite difficult to get any precision out of this at the end of the day. If the two or more theories are running in parallel, then

they will continue until some event or some discovery emerges that effectively puts an end to one of them?

A. They have continued beyond that.

THE CHAIRMAN: They continue beyond that? Yes. You mention the South African situation where possibly a political explanation is to be preferred over any sort of medical explanation.

A. Indeed.

THE CHAIRMAN: Do you want to follow that in any way?

MR DAWSON: No, thank you, sir.

THE CHAIRMAN: Mr Anderson?

MR ANDERSON: I have no questions, sir.

THE CHAIRMAN: Mr Sheldon?

MR SHELDON: No questions.

MS DUNLOP: May I ask --

Further Questions by MS DUNLOP

THE CHAIRMAN: I thought you might.

MS DUNLOP: Sorry, Professor Lever, just that last point.

Professor Ludlam's work in discovering this altered immunology in his patients who had been treated with concentrates, he is able to tell us that these were not people who went on to develop AIDS. Do you know if that end of the story is also possible for the population of homosexual men that was studied? In other words, was it possible to go back afterwards and say, "Well, in

retrospect they were all going to develop AIDS"?
A. As far as I'm aware, everybody who developed a lymphocyte subset mismatch in the gay population, who were HIV-infected carried on and progressed and developed immunodeficiency.
Q. I just wondered if there was a parallel with the haemophilia patients because the situation in the haemophilia patients, as we understand it, is that the altered immunology turned out to be a freestanding phenomenon, and whether that is also true of gay men. Did it turn out that independently of AIDS they had altered immunology?
A. I don't know for certain of any publication on non-HIV-infected gay men looking at their lymphocyte subset proportions, and I'm sure there is published data on that. So I confess my ignorance. I don't know.
Q. Right.
THE CHAIRMAN: It's likely to be quite a complicated position, isn't it, with cytomegalovirus and Epstein Barr virus having an impact on the immune system? Perhaps you have a very complex situation that would be very difficult to unravel; I don't know. Would there be immuno-suppression in most homosexual men because of other virus and other attacks on their systems?
A. It has certainly been talked about but I don't know for

certain of accurate epidemiological evidence to show that. One of the difficulties is, of course, that if you are in a group of individuals who expose themselves to a very wide range of infections, then statistically you are more likely to get infections. So actually quantitating whether the immune system was compromised by simply looking at how many infections the population get would reflect probably more exposure than innate immunity.

MS DUNLOP: Just a couple of other points not on that.

To go back to an answer that you gave to Mr Dawson towards the beginning of his questioning, you said that your own view around about May 1983 would have been that it was quite likely that there was an infectious agent transmitted by blood products and you imagined the situation of speaking to an audience where you would be trying to reassure. So I suppose the position I have just sketched, that this is quite likely to be an infectious agent transmitted by blood products, you would have expressed that view to a room full of people that you weren't aiming to reassure? But if you had been in a room full of patients with haemophilia, perhaps, and you held that view, objectively held that view, which is not a reassuring one, would you still have felt the need to reassure?

A. I think, as a medical practitioner, you should not unnecessarily alarm people. So it would be irresponsible just to give a message which simply frightened individuals without also expressing alternatives or covering statements, such as there may be an infection but we have no idea of the severity or how many people who get the infection would actually develop illness.

So as a general term, if one is dealing with a population -- and all patients to one extent or another are a vulnerable population -- we are all vulnerable populations -- I think it's one's duty to give information but in the least alarmist way one can.

So I think, if I was talking to a room full of people in whom the news might cause unnecessary alarm -- and at that stage one didn't know whether it was unnecessary alarm -- one would indeed have tried to cover one's message with as much reassurance as one could at the time.

Q. Just finally, this in a sense, follows from that. Mr Dawson developed with you the two different aspects of the risk/benefit analysis: one being the risk/benefit analysis as applied to the whole population and the risk/benefit analysis for an individual. On the question of the latter risk/benefit analysis, at that

time, I suppose, would it have come to, on the one hand the risk of getting this infectious agent which had a very high mortality versus, on the other hand, reverting to the risk of spontaneous bleeding, such as accompanies severe haemophilia? Would that be the choice?

A. Well, at the time one didn't know that the infection itself carried a high mortality. One knew that AIDS did. One didn't know that 100 per cent of the people who were infected developed AIDS and there wasn't a precedent for that in infectious diseases. So that would colour one's judgment slightly.

But if you look at perhaps comparable situations, and we are talking about a situation where the lifespan of the population had been extended by some 20 years over the course of not a dissimilar period of time, you would be looking at a situation similar to that in the treatment of many of the leukaemias, where again there had been massive increases in life expectancy. But people going into the treatment of leukaemia would know and would be told that there was a percentage risk of them not surviving.

So I think there are parallels in other situations. I don't think this is necessarily a unique situation, whereby the worst case scenario is not surviving.

I think there are a lot of other medical parallels where the worst case scenario is not surviving, but if that's for a very, very tiny proportion of the population, then the individuals take a decision for themselves as to whether they want to take that risk.

Q. That, in the early 1980s, would have been the principle, would it, that because there is a risk, albeit a small risk, of a fatal outcome, the danger is mentioned to the patient so that the patient can take the decision?

A. I think it depends on the history of the field you are dealing with.

Q. Right.

A. Certainly in the treatments for malignancy that would almost certainly be the norm.

Q. Thank you.

THE CHAIRMAN: Professor Lever, thank you very much indeed. It will take time to digest it all because some of the answers are very precise but the effort that you have put into it is really tremendous and I'm very, very grateful.

MS DUNLOP: Perhaps we could have our break now, sir.

THE CHAIRMAN: I think that might not be a bad idea.

MS DUNLOP: Yes.

(10.49 am)

(Short break)

(11.22 am)

Presentation of additional material by MS DUNLOP

THE CHAIRMAN: Yes, Ms Dunlop?

MS DUNLOP: Sir, at this point, which is obviously the conclusion of block 2, there are still one or two loose ends. I hope I have kept sight of all of them, although it's possible that I have missed something and other parties can always raise that, if they spot something else.

But to start with, something that I mentioned at the beginning of block 2, which is really I suspect, not a significant point, but it relates to a letter which is dated 11 January 1982. I had imagined that it could be seen as a significant letter because it refers to the arrival of heat-treated concentrates. The Inquiry team has come to the view that the date on the letter is probably wrong and that it's one of those January letters where someone has forgotten that it's a New Year and that the correct date is probably 11 January 1983. Could I very briefly run through the reasons on that?

The actual letter itself is [DHF0030892]. It's a circular letter and I can see that from another copy of it that we have, it is signed by Professor Bloom and Dr Rizza. We can see that it relates to at least four commercial companies who are about to introduce

preparations of Factor VIII, possibly Factor IX, that have been processed in an attempt to reduce the risk of transmitting Hepatitis B and non-A non-B.

The points that are particularly made, the numbered points, relate to the need for properly conducted clinical studies. Then onto the next page, if we could, please. There is data on the efficacy of the products and then at the end of paragraph 2 we have a reinforcement of the point that formal trial is important and, three, that use of products on a named-patient basis bypasses these regulatory controls.

If we look back to another document, [DHF0030059], this document is the minutes of a meeting at BPL on 15 December 1982. Again, this is a document of which we have another copy and we know certain personnel who were there: Dr Lane was there, Dr Cash was there and Professor Bloom was there certainly. This was a meeting discussing the advent of heat-treated concentrate. If we look on to the second page, we can see at the top a similar sort of thinking:

"The need for centralised, fully-controlled prospective trials of HS, hepatitis-safe materials, best operated through a properly executed national clinical trial."

And so on:

"Proposals. Random exploitation of the haemophilia service by commercial organisations for the study of hepatitis-safe products should be discouraged ... formal basis for controlled clinical trial."

And so on. Then the final document in this little chain is [SNB0135265]. Can we bear in mind that that meeting is 15 December and it's actually a meeting that's going to feature in block 4, when we come to study viral inactivation as a topic. But on 21 December there has been in fact an exchange of correspondence between Dr Cash and Dr Lane. This is Dr Lane writing back to Dr Cash. All I would like from this letter at this point is that one of the agreements at the meeting at BPL had been that Messrs Bloom and Rizza would be writing out to the haemophilia directors.

So putting all these things together, in fact there had been this meeting on 15 December, they had been discussing the need for properly controlled clinical trials. There had been an agreement at the meeting that Messrs Bloom and Rizza would write to all the haemophilia directors. The view of the team is that the letter of 11 January is that intended letter and that it only makes sense then if the date, 11 January 1982, is seen as a mistake and it's in fact 11 January 1983.

THE CHAIRMAN: At the moment in the preliminary report, paragraph 7.13 takes the date just as it is but paragraph 7.14 sets out the dates on which applications were made. They don't fit terribly well with a date of 11 January 1982 but I'm not sure they fit terribly well the date of 11 January 1983 either.

MS DUNLOP: Well, actually it was this that started the train of thought in the first place, that 11 January 1982 would have been very early to be saying there are four companies which are about to introduce products. If they were only applying for licences in America from June 1982 onwards, it seemed to us that on balance, January 1983 fits better than January 1982.

THE CHAIRMAN: Any views on that?

MR ANDERSON: I agree. I have nothing to add.

MR DI ROLLO: It does looks as though there are no other --

THE CHAIRMAN: It is a possible explanation even in the absence of the circumstantial material.

MR ANDERSON: It cannot be January 1982 whatever else it is. I don't think it can be January 1982.

THE CHAIRMAN: Just far too early, really.

MS DUNLOP: Yes. I should say, I had anticipated that this letter might feature and it hasn't really but it seemed possibly misleading in suggesting that heat-treated commercial products were available as early

as January 1982. So that was really the only purpose in saying that the team has come to the view that the date is probably wrong because it doesn't fit with the other evidence. Because I said at the beginning that I was going to return to that, I wanted to return to it.

THE CHAIRMAN: Right.

MS DUNLOP: So that's the first point. The second matter I wanted to close off, if I can, is the whole question of the funding of haemophilia centres, or more widely haemophilia treatment in Scotland, by drug companies.

The haemophilia directors who have given evidence were asked about it and they provided their own letters or statements. Those who haven't given evidence but who were also asked about it are for Aberdeen, Dr Bruce Bennett and Dr Audrey Dawson. Dr Bruce Bennett's letter is [PEN0150352]. Dr Bennett and Dr Dawson seem to have been co-directors in Aberdeen and he has provided a letter saying that to the best of his recollection:

"We received no funding whatever from commercial producers of Factor VIII."

Dr Dawson's is in fact the immediately preceding numbered document, [PEN0150351]. The other person who provided a letter about this topic is Dr George McDonald from Glasgow Royal Infirmary. His letter is

[PEN0150073]. It seems from the second paragraph of his letter as though it's not an unknown concept, financing for staff provided by pharmaceutical companies, but he does say in the first paragraph that as far as he can recall:

"No funding was received from pharmaceutical companies to employ staff in the department of haematology, Glasgow Royal Infirmary, for duties pertaining to the regional haemophilia centre."

The team made similar --

THE CHAIRMAN: The last paragraph there does talk about grants received from pharmaceutical companies.

MS DUNLOP: Yes.

THE CHAIRMAN: So there was a system to handle some grants.

MS DUNLOP: Yes. I don't know whether that perhaps refers to the sort of funding that the directors have spoken about, grants to facilitate attendance at conferences or the holding of the symposia in Glasgow. There were the two, the one in 1975 and the one in 1980.

THE CHAIRMAN: Yes.

MS DUNLOP: The Haemophilia Society has also provided information. Just for the record their letter on this topic is [PEN0150365]. Provided via their solicitors.

They have made such enquiries as they can at this remove and they have discovered one or two instances of

fundraising and a donation of £2,529 from pharmaceutical companies, a one-off donation for research purposes. Then perhaps we can go on to the next page, please.

So they are saying that they haven't found anything to suggest that there was general funding and they make the point that it's very unlikely that any funding from pharmaceutical companies would not be acknowledged within the bulletins.

With that letter they sent copies of various bulletins including the one that makes reference to the £2,000-odd donation. Perhaps we do not need to go to them but I think I should read out the numbers so that the numbers are in the transcript for anyone who wants to look at the bulletins. They are [PEN0150361], [PEN0150354], [PEN0150358], [PEN0150359] and [PEN0150360]. And that order is, as far as I can make it, chronological. I think running over a period from 1979 to 1985.

The third matter --

THE CHAIRMAN: Could I just find out what the reactions are to this?

Mr Di Rollo, do you have any position in relation to this material?

MR DI ROLLO: No. The letter, I think, is clear enough. There is nothing I would wish to add.

THE CHAIRMAN: I think that we do have material in Douglas Starr that perhaps is responsible for some of the questions around this arising but I have to go on evidence and I think it would really be for those instructing you to adduce evidence if you wanted to pursue this topic, but it may be that you simply accept the material that's here. I don't know.

MR DI ROLLO: Well, I don't think there is any other material that can be brought to bear or obtained. So I think it is as it stands at the moment.

THE CHAIRMAN: Mr Anderson, I'm almost tempted to not even bother asking you but do you have any point?

MR ANDERSON: No, sir.

THE CHAIRMAN: Mr Sheldon?

MR SHELDON: Nor I. The factual material speaks for itself.

THE CHAIRMAN: Thank you.

MS DUNLOP: I have four topics, sir, and that's the first two.

THE CHAIRMAN: You are suggesting that if I don't interfere, you will get on with it faster?

MS DUNLOP: Not in the slightest. I was going to apologise for the fact that number 3 is the longest one. It's just that it involves looking at some letters, I hope rather briefly. But I think it would be useful to look at them because they cast a little bit more light on

some of the mysteries about choice of products, particularly in Glasgow in the 1970s.

One of the team, still at Drumsheugh, has been doing a lot of research in this area and there is a series of letters, as always I suspect not quite complete, but if I could perhaps refer to them with apologies for not having supplied a list of them but they are all in court book.

The first is [SNB0070860]. This is going back to 1976. Dr Davidson, the haematologist at Glasgow Royal Infirmary, whose name has been mentioned on a number of occasions, is writing to Dr Wallace, the then director of the West of Scotland service, about Edinburgh intermediate Factor VIII. It certainly seems to be the name by which it was known in Glasgow.

It's referring to a rationing to 100 vials of Edinburgh concentrate per month. He says:

"We have had to supplement our Factor VIII with a fair amount of commercial product. We have recently started cautiously with home treatment using the Edinburgh product."

Essentially he is looking for more material.

THE CHAIRMAN: It is June 1976 of course, things are just getting into gear really.

MS DUNLOP: Yes, absolutely.

That letter was copied to Mr Watt and shortly after that Mr Watt writes to Dr Wallace. It's 15 June 1976, [SNB0070864].

Mr Watt, perhaps not being entirely encouraging about the suggestion of increased supply. Giving some explanations about some of the things that have been happening. Then going on to the second page, if we could, please. Dr Hopkins featuring also in this letter. He is hoping, at the top of the second page, to receive more fresh plasma from the West than has been possible and that could have a substantial effect on their ability to produce Factor VIII.

THE CHAIRMAN: Do you know whether at this time it was still on a population basis or was it pro rata to fresh-frozen plasma supplies or what? Or was it an artificial system?

MS DUNLOP: It's difficult to work out quite what the system was. If there was some sort of rationing of 100 vials a month, quite how that was arrived at, whether it correlated with population or number of patients or amount of plasma supplied. So far, we haven't found any information about that.

THE CHAIRMAN: The next paragraph, of course, deals with the cryosupernatant point which Glasgow resisted with all its vigour, so far as I can tell.

MS DUNLOP: But Mr Watt is saying that he finds it difficult -- this is the third paragraph:

"... to understand why Dr Davidson has had to supplement with a fair amount of commercial product. This can only mean that he has a personal preference for the commercial product or the actual rate of usage of Factor VIII has increased again in the west."

And wanting to know what sort of quantity is being referred to. Then at the end of the penultimate paragraph, a reference to self-sufficiency.

THE CHAIRMAN: He looks to have been very frustrated:

"We can hardly be accused of failure to meet clinical requirement if we are no allowed cover access to the information available."

MS DUNLOP: I imagine that the wording of the letter might have been corrected before it was sent out. It doesn't look quite right but this, I suppose, is a file copy.

THE CHAIRMAN: I suspect some of this is part of the dispute between Mr Watt on the one hand, and the haemophilia clinicians on the other, over whether there should be a haemophilia register and proper returns at that time of the products used. I get a sense that this is not a simple answer to the question of the volume of supply but --

MS DUNLOP: No, and I think he is making his feelings plain

when he says:

"We have all attended far too many meetings in discussion of the problem to reach at the present time what appears to be a point of total confusion."

So a degree of exasperation certainly.

THE CHAIRMAN: Yes.

MS DUNLOP: Then we move to a letter from October 1976, which is [SGH0029295]. This is Dr Wallace to Mr Watt and interesting because it refers explicitly to there being currently considerable competition between firms supplying Factor VIII concentrate:

"Some of these firms are offering substantial reductions for large orders."

Dr Davidson has raised the implications with Dr Wallace. Dr Wallace goes on to say to Mr Watt at the end of the second paragraph:

"Both he and I appreciate your many problems but we would welcome your present opinion."

Then in the last paragraph:

"I think they ..."

That's the doctors at the haemophilia centre and the Royal Infirmary:

"... would like to have a reasonable guarantee of 200 vials per month with the prospect of even more."

This is interesting, sir, because doing the best we

can to work out when Yorkhill became up and running as a haemophilia centre, and Dr Pettigrew's reference to the lack of a guarantee of supply, this all seems to be part of the background at that time. I think also too, the reference in the autumn of 1976 in this letter to commercial firms offering substantial reductions. Then November 1976, Mr Watt back to Dr Wallace, [SNB0070943]. Again, back to what were then current plans, recording his appreciation of the dilemma in which Dr Davidson may be placed by the competing interests of firms supplying Factor VIII concentrates.

Talking about current issues. Then on to the second page.

THE CHAIRMAN: Does that last paragraph suggest that there are process problems?

MS DUNLOP: Yes.

THE CHAIRMAN: That the capacity of the plant wasn't up to producing Dr Cash's estimate of the total amount required.

MS DUNLOP: It does look like that, sir, yes. I suppose yield, as so often yield is coming into it as well.

THE CHAIRMAN: Indeed. Yes.

MS DUNLOP: The second page, the reference you made a moment ago, sir, to the West of Scotland haematologists being reluctant to use the material produced by the processing

of the cryosupernatant. The puzzling reference perhaps to Dr Peter Jones. I'm not quite sure where he came in at this point.

THE CHAIRMAN: I have read this and the only inference I could draw was that in some way Mr Watt was in contact with Peter Jones to have the material trialed.

MS DUNLOP: Yes.

THE CHAIRMAN: It was clearly of lower potency than the other material but there is quite a lot of surrounding correspondence that suggests that even so John Watt believed that it could make a valuable contribution to the treatment of patients.

MS DUNLOP: Yes.

THE CHAIRMAN: That view was clearly not shared in the West of Scotland.

MS DUNLOP: Well, I think Dr Foster covers this in his paper as well and in the end it doesn't seem to have been something that was accepted.

Then he goes on to say, at the end of the penultimate paragraph, that:

"Both Dr Cook and Dr Cash ..."

I think this would be Dr Cash on behalf of Edinburgh, Dr Cook on behalf of Inverness:

"... are looking for increased supplies of Factor VIII concentrate."

Not a particularly easy sentence to interpret actually.

THE CHAIRMAN: No.

MS DUNLOP: "I suspect that initially the increased supply from the West of Scotland will be reflected to some extent by the increased satisfaction of the demand from the other two centres, since it will be less easy to resist their blandishment than hitherto."

THE CHAIRMAN: It must be the increased supply of FFP, mustn't it, plasma?

"Increased supplies of plasma for production."

He is going to have to use up some elsewhere.

MS DUNLOP: Yes. It looked to be saying: in the West of Scotland you may be going to supply more but I may have to use that to satisfy the requests from Inverness and Edinburgh. So don't imagine that you will get back a pro rata share of that material. It seems to be the point.

THE CHAIRMAN: But Dr Cook and Dr Cash are using blandishments to get more, whereas Glasgow had a more direct approach perhaps.

MS DUNLOP: Well, if nothing else, I think we can see that it was quite complicated. There is then, on 5 November, a letter from Dr Wallace to Mr Watt, which is [SGH0029294]. Dr Wallace is trying to send as much

fresh-frozen plasma as possible:

"My staff, like me, are hopeful that we can break the back of this Factor VIII problem."

Then December 1976 --

THE CHAIRMAN: Could we just pause on that? Is this question of SPPS something that I have to pay a lot of attention to, particularly the reference to the requirement for that particular product for burns therapy? I think my impression is that in due course it was accepted generally that alternatives to SPPS were acceptable to the people with particular problems, but is it something I have to look at or is it just part of the history that one needs to note but not develop?

MS DUNLOP: I would have thought, sir, that it's the latter, that certainly plasma was not exclusively available for the production of Factor VIII concentrate and that's perhaps all we need to take from it.

THE CHAIRMAN: Indeed. It's just another element then in the general equation of use of the source material. But at the moment I don't have any feel for whether the SPPS element in it is greater or less than the desire to use cryoprecipitate in the West of Scotland or to process cryo at Law Hospital.

MS DUNLOP: No.

THE CHAIRMAN: I just don't know. Overall the letter

suggests a joint approach is being adopted at that stage to reach some sort of agreement on targets for F8 products.

MS DUNLOP: Yes. Then Dr Hopkins comes in again. He writes on 22 December 1976 to Mr Watt.

THE CHAIRMAN: A typical letter?

MS DUNLOP: Not as colourfully expressed as some, other than the fact that he has had to do his sums by hand, which he remarks on. That's [SNB0070970].

This is another letter apparently dealing with shortfall really. The third paragraph:

"If we supplied 200 vials a month to Glasgow Royal and meet our current commitments to other hospitals, we may need a monthly average of something like 250 to 300 vials. Mr Grant has told me our current regional monthly quota is 100 vials."

So obviously a bit of a gap.

THE CHAIRMAN: John Davidson, what was his discipline?

MS DUNLOP: He is a haematologist in Glasgow Royal Infirmary and he at this point seems to be, as far as one can tell, performing the same sort of job as Dr Boulton. He is a bit of a middleman. He is not, as I understand it, a haemophilia clinician. He is not directly involved in treatment but he is trying to help, I suppose, with the supply issues. I think, looking back at the evidence

too, the position seems to have been that he may have been the person who did the order forms in Glasgow Royal Infirmary.

THE CHAIRMAN: But for the whole of the West of Scotland? Or for the infirmary alone or what? Do we know?

MS DUNLOP: The reference to other hospitals is puzzling because the only other hospital one can think of is Yorkhill.

THE CHAIRMAN: Unless they are using satellites in Paisley, Greenock and all the rest of it, to do some treatment. But the relative volumes would then worry one, wouldn't they?

MS DUNLOP: In terms of the contrast?

THE CHAIRMAN: Yes, 250 to 300.

MS DUNLOP: Yes.

THE CHAIRMAN: I don't think a computer would have helped him solve the problem.

MS DUNLOP: No. I suppose the context of all of this is was there a place for the purchase of commercial material. I think certainly it looks as though anyone wanting a guarantee of stock in the hospital at any given time might well have had to resort to the purchase of commercial material.

There is then a bit of a leap to 1977. The next letter I have is [SNB0071243]. This is

2 September 1977. Dr McDonald to Mr Watt. This is about the cancellation of a planned meeting to discuss the problem of the availability of plasma fractionation and the availability of Factor VIII products.

So quite what that reflects is really impossible to work out, I think, at this remove.

THE CHAIRMAN: Yes.

MS DUNLOP: Then Mr Watt contacted Dr Prentice when he saw the minutes of the haemophilia directors' meeting in 1977, in which Dr Prentice was recorded as having said that he had to buy commercial product. That appears to have leapt out at Mr Watt and he wrote to Dr Prentice about it on 12 January 1978. [SNB0017242]. Recording that he is actually distressed to discover that commercial Factor VIII has been purchased in Scotland during 1977.

THE CHAIRMAN: This is John Watt's theme really. "If you tell me what you want, I can do it but I need the raw materials", and so on. Yes.

MS DUNLOP: And I need information as well.

THE CHAIRMAN: Yes.

MS DUNLOP: Then very close in time, 18 January 1978, Dr Davidson to Mr Watt, [SNB0017237]. This is, I think, a direct response to the letter to Dr Prentice. Dr Davidson is sending a table which we haven't found.

No doubt it's in the database somewhere but it is probably decoupled from the letter and it won't have a date on it. A table giving the Glasgow Royal Infirmary blood product statistics for 1977. Actually the letter, I suspect, tells us much of what's in the table.

Interesting to note from the third paragraph that Edinburgh had supplied 1.2 million units to the West of Scotland in 1977. Of that, 0.7 million units had been used in the Royal Infirmary. So the remaining portion perhaps was largely used at Yorkhill. That would certainly be one explanation.

THE CHAIRMAN: Except that that's not really consistent with the last sentence in the third paragraph, that:

"The use of commercial F8 outwith this hospital, my guess is that it would be low enough to be left out of your calculations."

Where does that come from?

MS DUNLOP: Well, it looks as though Dr Davidson's perception of the situation then was that, whatever other hospitals than Glasgow Royal Infirmary were being supplied in the West of Scotland, were using mostly NHS material rather than commercial material.

PROFESSOR JAMES: This only gives Glasgow Royal Infirmary --

MS DUNLOP: Yes.

PROFESSOR JAMES: -- statistics. So presumably there is additional statistics for the Children's Hospital?

MS DUNLOP: Yes. He says:

"It will be a happy day when Scotland is self-supporting for all plasma fractions. It would be nice if this was in 1978."

THE CHAIRMAN: Yes, this doesn't really tell us who was buying what, how much was being bought, whether and how it was being recorded and so on.

MS DUNLOP: Well, it gives us a total usage for NHS product in the West of Scotland in 1977.

THE CHAIRMAN: With respect, it doesn't. It shows you supply and it shows you how much was used in the Royal Infirmary. We don't know whether there were stocks being built up elsewhere. Having regard to Dr Foster's evidence, it is not possible to exclude that at the moment.

MS DUNLOP: I suppose it is possible that the 0.5 million units, the half a million units were not used. I take that point, sir. Frustratingly, the statistics for Yorkhill only refer to amounts from 1980 onwards.

THE CHAIRMAN: Yes.

MS DUNLOP: So it's very difficult to know actually what the breakdown was between NHS and commercial product being used in Yorkhill in the late 1970s.

THE CHAIRMAN: So far, rather unfortunately, all of this material seems to be strengthening the impression that there was a lack of accountability, right across the system.

MS DUNLOP: Certainly the impression seems to be that it was quite a complicated problem, that people were in theory supportive of the notion of self-sufficiency but that perhaps in practice the supply was sometimes inadequate.

THE CHAIRMAN: Yes.

MS DUNLOP: The next letter we have is another one from Dr Hopkins from 1980. I appreciate that's quite a leap in time but it's [SNB0072612]. It's perhaps, sir, if you are wondering, medium colourful in its terms. I suppose, making the obvious point that fluctuating demand is always going to be a problem.

THE CHAIRMAN: Yes, could we just read it. I think the first paragraph is interesting:

"1,000 bags of cryo are issued each month, 200 plus or minus 100 to other hospitals in the region."

That indicates that the bulk of the material is being used in Glasgow and a relatively small proportion going to other hospitals, which contrasts quite markedly with the previous balance of 200 to 300 going out and 100, isn't it, being used in Glasgow?

MS DUNLOP: I think that was the vials of Factor VIII.

THE CHAIRMAN: Yes.
MS DUNLOP: Yes.
THE CHAIRMAN: I'm not looking at the particular material but just in the balance of usage, which doesn't immediately look right. Dr Hopkins' information from the period could be of wider interest in the Scottish executive, couldn't it?
MS DUNLOP: Well, not a problem that has gone away.

Just to look at the second page, what Dr Hopkins is planning to do with the cryoprecipitate stocks, wanting to therefore send more fresh-frozen plasma to Edinburgh and then at the end asking for warning if there is a supply problem coming. I think really referring to twin pressures: one, a sudden increase in cryoprecipitate demand or, two, a sudden drop in Factor VIII supplies from Edinburgh.

Then Mr Watt, a slightly reassuring response, 26 August 1980, [SNB0072614]. He says that they are getting better yields with their Factor VIII and increased issue from PFC does tend to result in increased availability of fresh-frozen plasma:

"Supplies are reasonably secure. It should be possible, given some disaster, to let you have at least two weeks notice of a likely hiatus in supply."

THE CHAIRMAN: I suspect it's "absent some disaster," rather

than, "given some disaster".

MS DUNLOP: I wonder if he was meaning -- given the text of Dr Hopkin's letter. Dr Hopkins was saying, "I need warning if there is a problem about to hit us". Mr Watt is saying that if something terrible does occur, "I should be able to warn you that it will bite in two or three weeks' time".

PROFESSOR JAMES: In the event of.

THE CHAIRMAN: In which case I really don't understand how it can have been taken as any comfort at all. We have a disaster. I will be able to tell you what's going to happen in a fortnight from now. It hardly let's one respond to the sort of incident that Dr Hopkins has in mind.

MS DUNLOP: Dr Hopkins only asked for ten days or a fortnight's warning. I suppose Mr Watt in that sense is saying, "I think I can give you a fortnight's warning".

PROFESSOR JAMES: This refers to a disaster at PFC, rather than a disaster on the terraces.

MS DUNLOP: I think that was all Dr Hopkins was saying:

"If Factor VIII concentrate supplies were suddenly going to fall, we would like to know about that and could I have at least ten days or a fortnight's warning?"

And Mr Watt seems to be saying, "I think I can manage that".

THE CHAIRMAN: Yes.

MS DUNLOP: Then 1981, a letter which I think we mentioned, sir, during the evidence, a letter of 24 April 1981 from Dr Crawford to Mr Watt, [SNB0071634]. This is the letter referring to Dr Davidson's policy of buying commercial products by rotation from a number of manufacturers. Actually, the letter goes on to deal with a quite specific point about the commercial producers having changed the labeling of their product. Saying on the label now that it's possible to store the product at room temperature for a short period. In essence, I think, Dr Crawford is saying it would be very helpful if you could say the same on your labels.

That's on page 2. He says:

"John would like to know whether it would be possible, on the strength of stability data you have on file, to modify the label to indicate for how long a period storage at room temperature would be acceptable."

A letter sent perhaps without much of an expectation of a positive response, but sent nonetheless.

THE CHAIRMAN: We can understand the difficulties. Storage on the shelf possibly is much more likely to happen when

somebody is on holiday than when they are at home.

MS DUNLOP: This is again speculating, but if patients were saying, "I really prefer this product from the X pharmaceutical company because I know I can take it on holiday and I don't need to keep it in a fridge all the time", then that small point of itself is going to lead to a preference by patients for the commercial product unless the NHS product is seen to afford equivalent flexibility.

Then finally, just really because it fits with Dr Foster's evidence -- and it may be that he has this in his reference list in his paper anyway -- a letter from 1982, [SNB0073184]. Dr Foster to Dr McClelland. This is a letter which is in the preliminary report as well, about quality considerations. Dr Foster says his initial reaction to the claim that PFC Factor VIII concentrate is a poorer quality than commercial intermediate purity products is that this is probably fair comment.

Referring to the need, which, as he explained himself, hit NHS producers in a way it didn't hit the commercial producers, to maximise yield in the pursuit of self-sufficiency.

Some very technical analysis on the second page of how the PFC product actually compared to some of the

commercial products.

I'm not sure, sir, in the end, how much light any of this material sheds, but perhaps it is no more than straws in the wind at the time about what the factors were, about the presence of the commercial suppliers in the marketplace and about concerns to do with reliability of supply, about the dynamic of how much plasma is supplied for what purpose and how much you get back in return. So I think all of these themes are reflected in the correspondence, but I suspect in the end it's impossible to put together a complete picture of what was happening.

THE CHAIRMAN: A factor that has been growing at least in my mind as one of importance is the way demand was changing.

MS DUNLOP: Yes.

THE CHAIRMAN: As the approach to therapy altered, it is fairly clear that the demand for products was changing in what perhaps was an unpredictable way, and if that is happening at the same time as there are independent factors affecting supply, then it could become extremely difficult indeed to correlate one with the other.

It may be that there is simply no resolution possible now to the problem. It's a great pity that Mr Watt didn't survive and that indeed he was too ill to

help us because I have no doubt he would have views which would probably be expressed quite forcefully but --

MS DUNLOP: I think one of the things that perhaps comes across from the correspondence is that in reality it would have been helpful to everybody to have a very large reserve stock at any given time because a number of these problems could have been alleviated by knowing that there was a decent amount of material held somewhere. Whether it was ever possible to receive plasma in sufficient quantities to set that up, I think is questionable.

THE CHAIRMAN: It looks as if it may have become possible, 1983/1984, but that was on the back of very considerable alterations to the plant and equipment at PFC. It may not have been possible before that to do it.

MS DUNLOP: Yes, and a whole raft of quite imaginative measures to achieve every last drop possible and make the best possible use of every donation, which all I gather will have taken time to feed through.

THE CHAIRMAN: Yes.

MS DUNLOP: The fourth point, sir, in conclusion, was just that we did refer to not having had any input from Dr Mitchell in this area. It's our intention to write to Dr Mitchell and perhaps put some questions to him

about his involvement in securing an adequate supply of PFC product for the hospitals in the West.

THE CHAIRMAN: The other two loose ends that I can think of immediately are Professor Hann and Dr McClelland; who were cut short, as it were one way or another. Do we have plans in hand to bring them back or are they going to be sort of built in at some stage?

MS DUNLOP: They are both on the timetable for block 3, sir. I can't, off the top of my head, give the dates but I know that they are pencilled in. They are scheduled to return.

THE CHAIRMAN: Gentlemen, this question of supply. As you will know from the preliminary report, I at least had a sense of frustration that the flow of data around the system made planning of production and supply very difficult. I'm not sure that the material is available now to resolve the difficulties.

Do you have anything to say on this at all, Mr Di Rollo?

MR DI ROLLO: Not at this stage, no.

THE CHAIRMAN: No.

MR DI ROLLO: I don't think there is anything I can usefully add to the material that you have.

THE CHAIRMAN: Out of this, I think, comes an impression that one way or another those at the front end had

a perceived need to use commercial products, which might be attributable to a whole number of things, starting with personal preference and ending up with the need to plug a gap in the public supply. I just don't know where we are on that. I would like you to think, not immediately, but think where you want to take me in that area. Again, it's Yorkhill that becomes the particular focus for it.

MR DI ROLLO: Yes, certainly.

THE CHAIRMAN: Mr Anderson?

MR ANDERSON: I don't think I have any comment at this stage.

THE CHAIRMAN: At this stage.

MR ANDERSON: I will clearly bear in mind your comments.

THE CHAIRMAN: It is a problem area. Unless one can find some credible explanation for it, then it's going to hang in the air --

MR ANDERSON: One thing I will do is to ask those instructing me to make further investigations to see if there are any other individuals who may be able to cast light on that. I suspect that may be a fruitless --

THE CHAIRMAN: We are looking a long time into the past and it may be fruitless but those instructing you do have to remember that John Watt made a very serious effort to persuade the haemophilia doctors in particular to

provide him with the sort of information that would have given us an audited trail of all the material needed and its use. The inability to answer questions now may not be entirely unconnected with that. The additional information that when commercial supplies were eventually returned, they were returned through the offices of Dr Ludlam, who in effect seems to have aggregated information and therefore deprived it of any real meaning, doesn't help. So if those instructing you can look at this again, I would be very grateful.
I would rather have an answer than a considerable hole that can only fuel speculation.

MR ANDERSON: I simply say that I will discuss it but without being terribly optimistic about it. We will certainly do it.

THE CHAIRMAN: We have been at it for a long time. I would be surprised that you would express optimism now that hadn't already been satisfied in other ways.
Mr Sheldon?

MR SHELDON: Nothing I can add at this stage, sir, thank you.

THE CHAIRMAN: Ms Dunlop, I still look forward with some hope, if not optimism, to finding an answer. But let's wait and see.

MS DUNLOP: We have no further business at the Inquiry

today, sir.

THE CHAIRMAN: Thank you all very much.

(12.21 pm)

(The Inquiry adjourned until Tuesday 7 June 2011 at 9.30 am)