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Wednesday, 15 June 2011

(9.30 am)

THE CHAIRMAN: Good morning. Now, Mr Di Rollo?

MR DI ROLLO: Sir, I just wanted to raise an issue which has been of some concern, which is the fact that documents are being lodged in court book at a late stage before the witness is giving evidence and that's creating difficulties for us in order to absorb the information and be in a position to make a meaningful contribution to proceedings.

Today's witness' report was lodged on Friday and we had not seen it until, essentially, the weekend. We haven't intimated questions. We have not --

THE CHAIRMAN: I'm not sure that I'm particularly sympathetic to the view that you had something over the weekend and are complaining. My recollection is that that's when I did most of my work, Mr Di Rollo.

MR DI ROLLO: We had other work to do over the weekend in relation to other witnesses. This is quite a busy week for us.

THE CHAIRMAN: What specifically? I can't deal with things in general. If you are disadvantaged, you must ask for an adjournment so that you can read the material, because you do have to be prepared, and I don't think anyone would deny that.

1           I don't myself keep a track of when documents come  
2           in and when they go out, so I don't know, but is there  
3           something specific that's concerning you today?

4 MR DI ROLLO: Well, I don't know, is the answer to that.

5 THE CHAIRMAN: Then I'll adjourn until you find out. You  
6           can have discussions with Ms Dunlop -- and I do want  
7           specifics, please; a general complaint doesn't help and  
8           if the Inquiry is going to be held up, it has to be on  
9           substantial bases and I would expect you to tell me what  
10          they are.

11         (9.39 am)

12   (Short adjournment)

13         (9.55 am)

14 THE CHAIRMAN: Are you taking the lead, Ms Patrick?

15 MS PATRICK: I am, sir, yes. If I could start by providing  
16          a bit of background and to why and how Professor Leen  
17          came to be instructed.

18                 He was identified as a witness by the Inquiry  
19                 in April and contact was made with him then. A draft  
20                 report was then received by the Inquiry and I then  
21                 consulted with him after that and his final report came  
22                 in to the Inquiry last Thursday.

23                 In an ideal world it would have been intimated  
24                 earlier but the purpose of Professor Leen's evidence is  
25                 to assist everyone here in relation to the effects of

1 treatment and what he is speaking to should not really  
2 be contentious.

3 THE CHAIRMAN: Right. So, as you understand it, the whole  
4 issue revolves around Professor Leen, does it, at the  
5 moment, because I have not yet had clear specification  
6 from Mr Di Rollo as to what the problem is?

7 MS PATRICK: I think we are looking at trying to proceed  
8 this morning and proceed with hearing the evidence of  
9 Professor Leen, and so what has been agreed is that we  
10 will proceed to hear his evidence and should any of the  
11 core participants have any questions arising out of  
12 that, they may ask those questions either at the end of  
13 his evidence or provide them in writing at a later date.

14 THE CHAIRMAN: Well, I'm not terribly keen on the idea of  
15 written exchanges after the evidence. There is  
16 a tremendous advantage in hearing the response to the  
17 question as it is put. But if that's what's agreed, and  
18 I'll go along with that for the time being and we will  
19 see how we get on.

20 MS PATRICK: Thank you, sir.

21 THE CHAIRMAN: Mr Di Rollo, you mustn't be disadvantaged and  
22 I am not really happy about compromises that leave you  
23 exposed to the feeling that you have not had the  
24 opportunity properly to prepare.

25 So I really do expect you, if issues of this kind

1           arise, to make sure that they are drawn to my attention  
2           and we will decide whether the Inquiry does have to be  
3           adjourned.

4           There will be times and circumstances, I suppose, in  
5           an Inquiry like this when everyone gets material late  
6           and people's capacity to respond will vary and I have to  
7           have regard to that.

8           But the time for focusing it is when the issue  
9           arises and I repeat what I said earlier: I'm not  
10          interested in generalised complaints from any of you.  
11          It has to be specific and I have to have the opportunity  
12          to take a decision in the light of what's said, whether  
13          the Inquiry should be interrupted, and I would only want  
14          to do that in extreme circumstances but if that's the  
15          right way to ensure that the issues are properly  
16          explored, then that's the way it has to be.

17          But I think I really would like from now on to have  
18          these things done formally and we will discuss them  
19          openly. I do not want to have further letters behind  
20          the scenes of a generalised nature, making complaints  
21          that can only be relevant if they have to be resurrected  
22          at some later stage, when someone might want to  
23          criticise the Inquiry processes, and I will be quite  
24          open about that with you.

25          From now on these things will not be done by

1 exchanges behind the scenes and I say what I said to you  
2 the last time: I'm still not yet closing the door on  
3 simply publishing everything that has transpired of late  
4 to ensure that the Inquiry's procedures are seen by  
5 the public at a time when remedial action can be taken  
6 if required. I'm not exposing myself to the risk of  
7 belly aching and complaining after the procedure is  
8 over.

9 So --

10 MR DI ROLLO: That wasn't the reason why I made the  
11 observation this morning.

12 THE CHAIRMAN: My comments are not directed at you alone.  
13 I just want everyone to be aware that I from now on will  
14 expect issues of procedure to be dealt with openly. And  
15 I'm quite fixed in my intention that that should be the  
16 case. Anyway, for the time being are you content to go  
17 today?

18 MR DI ROLLO: I'm content to go with this witness and  
19 perhaps we should deal with that. There is another  
20 matter relating to the next witness but perhaps we could  
21 deal with that --

22 THE CHAIRMAN: We will deal with that once we have finished  
23 Professor Leen.

24 MR DI ROLLO: Thank you.

25 THE CHAIRMAN: Very well.

1 PROFESSOR CLIFFORD LEEN (sworn)

2 Questions by MS PATRICK

3 MS PATRICK: Good morning, Professor Leen. I would like to  
4 start by looking at your curriculum vitae, which you  
5 provided to the Inquiry. It is PEN0010955. Have you  
6 got a copy of that in front of you?

7 A. Yes, I do.

8 Q. On page 2 you list your education and qualifications and  
9 we can see that you obtained your medical degree and  
10 an MD at Edinburgh?

11 A. Yes.

12 Q. You became a member of the Royal College of Physicians  
13 in 1982 and then a fellow both at Edinburgh and London  
14 thereafter. If you scroll down, please, you tell us of  
15 your involvement with the British HIV Association and  
16 you have been involved as a member of the guidelines  
17 subcommittee and thereafter in various other capacities?

18 A. Yes.

19 Q. Can you tell us about that association?

20 A. So the British HIV Association was set up for people  
21 caring for patients with HIV. So it has doctors,  
22 nurses, pharmacists and virologists as well, okay? So  
23 there are about 900-odd members in the UK.

24 Q. Okay.

25 A. So we have meetings, it's all about education of HIV for

1 carers, mostly for carers, as opposed to patient  
2 information. But there is some patient information as  
3 well.

4 Q. Okay. When did that association first come into being?

5 A. It probably would have been in the early years. I can't  
6 remember exactly when but I joined it as a member  
7 initially in about 2000, when it held its first meeting  
8 in Edinburgh.

9 Q. Thank you. If we go over to page 4, you list there your  
10 previous positions, as you work your way up. We can see  
11 that you worked in Edinburgh. If we scroll down, in  
12 1984 you were a research registrar at the Regional Blood  
13 Transfusion Service?

14 A. I was, yes.

15 Q. What did your work there involve?

16 A. I was attracted to join the research there because we  
17 were trying to find a way of treating patients with  
18 gram-negative sepsis, septicemic shock. The plan was to  
19 try and identify plasma that we might be able to use to  
20 try and reduce some of the toxins in the blood. That  
21 was the idea. But what happens quite often, things  
22 don't pan out as well, and my research changed a bit.  
23 So I was looking at procurement of hyperimmune plasma,  
24 ie full of antibodies for tetanus, for rubella and  
25 things like that.

1 Q. So it didn't go exactly the way you planned when you  
2 first arrived there?

3 A. No.

4 Q. Then we can see that you were a senior registrar in  
5 Manchester and spent time there -- if we go over the  
6 page -- and in London, before returning to Edinburgh  
7 in May 1989?

8 A. Yes, it is.

9 Q. You then became a consultant physician of HIV Infectious  
10 Diseases initially at City Hospital and then at the  
11 Western General Hospital?

12 A. The hospital closed down and we moved the unit to the  
13 Western.

14 Q. When was that that it closed?

15 A. That was in 1998, the summer of 1998.

16 Q. Then if we return to page 3, you tell us about your  
17 current position, which is still consultant physician in  
18 infectious diseases and now honorary professor in the  
19 department of medicine at the University of Edinburgh.  
20 You treat community-acquired and hospital-acquired  
21 infections and have a special interest in blood-borne  
22 viruses, and you tell us that you are the lead clinician  
23 for blood-borne viruses in the unit.

24 A. Yes.

25 Q. Do you mainly see patients with HIV?



1 A. I do, yes. I treat them as well.

2 Q. Yes. Does that make up the greatest proportion of your  
3 patients?

4 A. It is probably coming to about 50 per cent of my  
5 workload in terms of time that I have spent caring for  
6 patients.

7 Q. So how long have you been treating patients with HIV?

8 A. Since 1986, when I started as a senior registrar in  
9 Manchester. The first day I started there in January,  
10 I was asked to help look after a patient with AIDS.  
11 That was interesting.

12 Q. You tell us about that further down page 3. Did that  
13 start your interest in the condition?

14 A. No, my interest was before that. I heard about HIV and  
15 AIDS certainly -- not so much about HIV but about AIDS  
16 initially. In actual fact, it's like 30 years since the  
17 first case of AIDS was reported in the literature. And  
18 it was the ultimate challenge for any infectious disease  
19 doctor because there you have a patient whose immune  
20 system is decimated by something, obviously HIV, and the  
21 challenge was to treat all the infections which arise as  
22 a result of this diminished immune system. That was the  
23 challenge.

24 Q. Yes.

25 A. Obviously the ultimate challenge was to find treatment

1 for HIV, or at least treat the patient with HIV with  
2 anti-HIV drugs, and that was coming along. So  
3 1986/1987, the first drug was available.

4 Q. Yes. If we carry on through your CV, you list on page 6  
5 your membership of research steering groups, your  
6 research interests, which includes the evaluation of  
7 antiviral drug resistance. Under "past appointments"  
8 you tell us that you served on the Expert Advisory Group  
9 on AIDS, to advise the four chief medical officers on  
10 matters relating to HIV and AIDS. That was between 2007  
11 and 2011.

12 A. I think it may be 2008. It may be a mistake, I'm sorry,  
13 but I can't remember. But it was so blurry. But it is  
14 a fixed period of appointment, yes.

15 Q. Over the page --

16 A. I apologise for that.

17 Q. Over the page at page 7 you were a member of the  
18 Scottish Office Clinical Resource and Audit Group,  
19 looking at the use of clinical resources in early HIV  
20 infection.

21 You then tell us your publications that you have  
22 been involved in, which is an extensive list. Those you  
23 contributed to are 132 in number. There are some  
24 further publications that you participated in but you  
25 are not listed as an author and these, it's fair to say,

1 are mostly HIV-related?

2 A. The majority of them, certainly, within the last sort of  
3 15/20 years.

4 Q. Initially there are some articles in relation to non-A  
5 non-B hepatitis, which was obviously an interest as  
6 well?

7 A. Yes. I was treating patients with primary antibody  
8 deficiency and they needed some immunoglobulins which we  
9 had to give them. The concern was whether or not some  
10 of them may be acquiring hepatitis viruses.

11 Q. Right.

12 A. That's a long time ago.

13 Q. Yes. You tell us at page 25 of your presentation at  
14 clinical meetings, and these are mostly in relation to  
15 the British HIV Association, the meetings over the  
16 years?

17 A. Yes.

18 Q. On page 33 you tell us of research grants held and these  
19 include grants from the Scottish Office, looking at the  
20 development of drug resistance in HIV infected patients,  
21 receiving combination antiretroviral therapy and an  
22 evaluation of immune recovery in HIV-infected patients  
23 treated with combination therapy.

24 You then list studies which you have been involved  
25 with. If I could refer you to page 38. One of these is

1 number 44, the long-term follow-up of all HIV infected  
2 persons seen since 1996 in seven major UK centres. Is  
3 that still ongoing?

4 A. Yes, I mean, we have received further funding to extend  
5 the follow-up. That's the UKCHIC yes, HIV cohort in the  
6 UK.

7 Q. You tell us at the end about your teaching and training  
8 and on page 42 we can see that in 2004 you obtained  
9 accreditation from the European AIDS Clinical Society to  
10 use the HIV unit in Edinburgh as a training facility?

11 A. Yes.

12 Q. You since trained doctors from other countries in  
13 respect of treatment of HIV?

14 A. Yes.

15 Q. Thank you.

16 I would like to refer you now to your report, which  
17 is [\[PEN0121044\]](#), firstly to page 2, basically to the  
18 second paragraph there.

19 You tell us that the first consensus statement on  
20 HIV treatment was issued by a panel of US experts  
21 following a conference on -- you might have to help me  
22 with the pronunciation -- Azidothymidine?

23 A. Yes, the other name is Zidovudine. That's the first  
24 drug that ever became licensed for treating HIV or AIDS  
25 patients --

1 Q. Yes. That conference was in 1990?

2 A. Yes. It was in the USA.

3 Q. When you say the "first consensus statement", what do  
4 you mean by that?

5 A. I think, before this drug was licensed, there were some  
6 studies on this drug. There was no other treatment for  
7 HIV, so when the drug first came, the first question  
8 was: how best do we use the drug? Should we use it in  
9 everyone with AIDS? The answer is probably yes. And  
10 then what about those people who are HIV positive but  
11 haven't developed AIDS?

12 So this would be to look at how to best use this  
13 drug. That was set up by the Americans to try and have  
14 a group of experts and have their views on how best to  
15 do them. That was the first real meeting of people  
16 working in the field to try and formulate, sort of  
17 recommendations, sort of guidelines type of things.

18 Q. Would that have been followed in the UK?

19 A. Not necessarily but those people in the know would  
20 probably want to see what views were expressed and then  
21 use their own judgment as to which bit to follow.

22 Q. Yes. You tell us there that the panel there concluded  
23 that a large proportion of the asymptomatic and mildly  
24 symptomatic HIV-affected population were candidates for  
25 early therapy with Zidovudine.

1 A. Yes.

2 Q. Then you tell us further down the page that the first  
3 British consensus on the treatment of HIV appeared  
4 in April 1997 in the Lancet, and thereafter was quickly  
5 revised and British guidelines were then produced from  
6 2000 onwards. Before that time, were there any  
7 consensus statements or guidelines in Britain that  
8 clinicians could follow?

9 A. None at all. Between sort of 1990 to 1996 there was  
10 lots of activity, looking at finding candidate drugs  
11 which might be useful.

12 Q. Yes.

13 A. There was a lot of knowledge arising as well in terms of  
14 how to look at the progression of HIV, predictors of  
15 progression, and also there was a new technology which  
16 was being used in the labs, which was looking at  
17 measuring the amount of virus there is in the blood.

18 So with this sort of activity, guidelines sometimes  
19 cannot keep up with the pace of new discoveries or new  
20 knowledge coming out, but I think around the mid-1990s  
21 there was so much happening that there needed to be  
22 guidelines because otherwise clinicians might be doing  
23 their own thing, which may not necessarily be the right  
24 thing for the patient.

25 So the founding chair of the British HIV

1 Association, Professor Gazzard, set up the meetings of  
2 the HIV Association, a group of clinicians and then  
3 discussed all the findings, by which time people were  
4 already looking at using two drugs as opposed to one  
5 drug, people were looking at whether or not they should  
6 sequence the drugs, but by 1996 a new drug class came  
7 up.

8 Q. Yes, we are going to come on to that.

9 A. That changed the whole face of HIV. And I think there  
10 was a need there because there was so much choice of  
11 antiviral drugs, how best to use it in order to ensure  
12 that the patient benefits from all of this.

13 Q. Yes. What I would like to do now is to get a picture  
14 from you of treatment when the virus first appeared in  
15 the 1980s.

16 If we return to page 1 of your report, presumably  
17 patients were tested for HIV when the test became  
18 available and were told that they were HIV positive and  
19 then were they continually monitored? What happened  
20 then?

21 A. Patients presented in two fashions. If they have some  
22 condition which then prompted the clinicians to do the  
23 test, then obviously the treatment for the condition  
24 presented with should be sorted out. With pneumonia,  
25 for example, or thrush or a viral infection.

1 Q. Yes, you tell us that here.

2 A. A list of things, lots of things there. So that will be  
3 treated. Obviously, if they have an AIDS-defining  
4 condition, as defined by, again the conditions which we  
5 don't see in patients with a normal immune system, then  
6 they would automatically be offered Zidovudine, which is  
7 the only drug available. That was available from 1987  
8 onwards, although some patients were able to access this  
9 drug from the time the study was finished and the whole  
10 process of licensing.

11 So that was straightforward. What was more  
12 difficult and less straightforward was: should you use  
13 the only drug you had in those patients who are infected  
14 but showing no signs of disease or of any HIV related  
15 problems? That was the big debate, and we knew that was  
16 an important issue because the benefit we got from using  
17 Zidovudine alone in AIDS patients was limited. So it  
18 was one bullet you had. When is it best to use that  
19 bullet? That was the dilemma that all clinicians had at  
20 the time.

21 Q. Yes. You tell us in the first paragraph that we are  
22 looking at here that in the early 1980s, when  
23 an HIV-infected patient was diagnosed, this patient may  
24 well have been cared for by the physician who made the  
25 initial diagnosis, so there were various different types



1 of doctors treating the virus at that time?

2 A. Quite likely, yes.

3 Q. Yes. You list some there and I take it, if it was  
4 a child, then it might be a consultant paediatrician?

5 A. It would be, yes.

6 Q. So how would these clinicians have known in the early  
7 days how best to treat HIV or AIDS?

8 A. Well, that is very difficult to be sure because I think  
9 any clinician who has a patient with AIDS, should really  
10 keep up with the literature and they will be reading the  
11 literature, and luckily enough in those days the  
12 literature was not very extensive, so it was easy to  
13 catch up, sort of thing.

14 I have to say, also sometimes, because patients  
15 present with a condition, if the clinician didn't think  
16 of HIV, then that condition could have been treated and  
17 HIV was missed --

18 Q. Yes.

19 A. -- until much later, when other conditions came up,  
20 other opportunistic infections came up.

21 So that's the problem about not having a speciality  
22 of its own, a disease which is just coming up and  
23 clinicians, they want to do their best for the patients  
24 and some patients' clinicians may not wish to refer and  
25 it was an area of uncertainty and I can understand why

1 sometimes it would be very difficult to know what was  
2 going to be done.

3 But having guidelines does help in terms of  
4 channeling and getting the right referrals for the  
5 patient.

6 Q. But there weren't any guidelines then?

7 A. There weren't any guidelines.

8 Q. So a patient's treatment may depend on the clinical  
9 experience and the knowledge of whichever doctor  
10 discovered that --

11 A. Diagnosed the patient's conditions, yes.

12 Q. You tell us further on in your report that nowadays and  
13 since 1993, outpatient care for HIV patients is either  
14 at the infectious diseases unit or at the GUM unit?

15 A. That's the majority of cases. It's very difficult. If  
16 let's say, a patient doesn't wish to be seen in those  
17 two clinics because of the connotation of HIV --  
18 patients do worry about that -- some clinicians may be  
19 forced to just keep looking after this patient but  
20 obviously asking for help from an HIV specialist from  
21 elsewhere, maybe, to try and monitor the patient.

22 Q. Yes. You tell us that in Edinburgh, for example, one of  
23 your colleagues held joint clinics with the haemophilia  
24 doctors, to keep clinic visits to a minimum, and  
25 obviously that would have avoided the necessity for

1 a patient with haemophilia coming to the infectious  
2 diseases unit.

3 A. Yes.

4 Q. Are you able to say when those joint clinics started?

5 A. No, it was before my time probably because the  
6 haemophilia group was one of the earlier groups to be  
7 recognised as being at risk from HIV and AIDS. But it  
8 may well have been very early. My colleague who did  
9 that is Dr Brettle who has retired a year or so ago now.  
10 So I haven't asked him that but it may well be very  
11 early.

12 Q. I would like to refer you now to page 6 of your report,  
13 where you tell us about the development and changes in  
14 treatment for HIV and AIDS over the years. You have  
15 already told us that Zidovudine was the first HIV drug  
16 approved for use in patients with AIDS. When you say it  
17 was approved for use, how was that approval made known  
18 to clinicians?

19 A. Well, there would be first of all clinical studies,  
20 which showed that it was beneficial. That would be  
21 published in the literature. And obviously that was the  
22 only thing available and clinicians looking after HIV  
23 patients would then know that the regulatory authorities  
24 would be assessing the quality of evidence and approving  
25 that drug and then anyone who is looking after HIV

1 patients would have known that this would be available  
2 because they would have been reading about this and  
3 ensuring that any advances that were known, they could  
4 access that for the patients.

5 Q. You refer there to a study which showed that you had  
6 a longer rate of survival on Zidovudine and that your  
7 rate of opportunistic infections was reduced. Do you  
8 know the date of this study?

9 A. I don't know exactly. I don't have the exact date but  
10 it would be around 1986 onwards, because late 1986  
11 certainly some patients were able to access this on  
12 a named-patient programme, but the date published would  
13 have been in 1986 and the licensing came in 1987.

14 Q. So the first patients to receive Zidovudine would have  
15 received it as a named patient?

16 A. They would have or as part of a clinical trial, but  
17 I think the trials were done in the US and therefore in  
18 the UK it would not be available.

19 Q. Can you explain what you mean by a "named-patient  
20 basis"?

21 A. Well, if I have a patient who I think needs a certain  
22 medication, then I could request access to this patient  
23 from the makers of that drug to see if they would be  
24 happy to provide these drugs before a licence for using  
25 that drug is available. That's the named-patient

1 access. There is now a very strict control of how they  
2 will allow the use of these drugs. There are very  
3 strict criteria that they would want followed and then  
4 they will release the use of those drugs.

5 A clinicians may well have to fill in forms, look at  
6 side effects and certainly will have to report any  
7 adverse effects, anything like that, to ensure that it  
8 is used safely and wisely.

9 Q. Right. So when you are considering treatment for  
10 a patient, the options open are a licensed drug, a drug  
11 provided on a named-patient basis and thirdly a clinical  
12 trial?

13 A. Yes.

14 Q. Which, as you say, is subject to strict regulations and  
15 presumably strict criteria for taking part in that?

16 A. Very much so.

17 Q. Were patients treated with medications that were part of  
18 a clinical trial in the 1980s for HIV?

19 A. Probably not, to my knowledge. I think later on there  
20 would be other studies done in the UK in order to look  
21 at how best to use medication. So probably it would be  
22 late 1980/early 1990s.

23 Q. You tell us further on in your report that Zidovudine  
24 was associated with an improved prognosis for no more  
25 than two years after starting therapy.

1 A. For patients with AIDS, late stage disease, yes.

2 Q. Was that any different if the patient had not yet  
3 acquired AIDS?

4 A. I think the benefit will wane over time and the reason  
5 is that the HIV virus is a very dynamic virus, which  
6 replicates very much. It is thought that up to  
7 2 billion copies of the virus is actually produced every  
8 day. A huge turnover.

9       What happens is there is a lot of mutation in the  
10 virus and when there is mutation, there is a risk of  
11 resistance to the drugs. So basically the virus changes  
12 into a virus which can still multiply in the presence of  
13 the drugs. So therefore, if you were to use it earlier  
14 in the disease, the resistance will still occur because  
15 Zidovudine isn't strong enough on its own to stop the  
16 replication of the virus completely. That's what we  
17 learnt in the years since when starting to use  
18 Zidovudine in 1987 routinely to, sort of, the early to  
19 mid 1990s. We knew that whatever we had in our weaponry  
20 it was limited, unless of course we knew how to use it.

21       It was only when one understood the rapid dynamic  
22 replication of the virus, how much the virus can mutate,  
23 how weak the early drugs were, and we knew that it's  
24 only by combining two drugs -- two drugs wasn't enough;  
25 three drugs was the minimum in the mid 1990s -- that

1 allowed the virus to be suppressed, to stop the mutation  
2 at the kind of rate to allow the efficacy of the  
3 treatment to be maintained over long periods of time.  
4 That was the turning point, in the mid 1990s.

5 Q. So in relation to treatment with Zidovudine in the late  
6 1980s, would that have been a difficult decision for the  
7 clinician to make, when to start that treatment?

8 A. It would be for those people who are still asymptomatic  
9 or very mildly symptomatic. Those who have AIDS -- as  
10 defined by one of the 12 conditions which we call AIDS,  
11 because they are quite severe conditions -- there was no  
12 doubt that they should be offered it because the risk of  
13 dying much outweighed the risk of giving it.

14 Zidovudine was associated with quite significant  
15 side effects as well because of nausea, headaches,  
16 vomiting. It also caused anemia and low white cell  
17 count, which are all already present in lots of patients  
18 with AIDS anyway, and there was a lot of bad publicity  
19 on Zidovudine in those days as well.

20 There was a programme on television showing that it  
21 was toxic and that clinicians were being rushed in using  
22 it and patients sometimes saw their friends taking  
23 Zidovudine and dying and therefore associated the death  
24 and the cause of the death to Zidovudine. So there was  
25 a major struggle even though we felt that it was

1 a useful drug. There was still a lot of resistance  
2 among some patients to take that. Whether or not it was  
3 only about the side effects or also the connotation,  
4 reminding them that they have HIV and AIDS, is unclear  
5 but certainly there was a lot of resistance in some  
6 patients.

7 Q. Yes. It wasn't until quite a few years later that more  
8 drugs became an option or different drugs became an  
9 option. You tell us at page 3 at the top that between  
10 1987 and 1993, two additional HIV drugs, Didanosine,  
11 which is also known as DDL. Is that right?

12 A. DDI.

13 Q. DDI and Zalcitabine, DDC, were undergoing clinical  
14 trials. Where were these clinical trials taking place?  
15 Were they in the UK?

16 A. Some of them might have been in the UK but a lot of them  
17 would have been in the US.

18 Q. Right. So when would patients in Scotland first have  
19 been treated with either of these drugs?

20 A. Again, once we knew that there was evidence of benefit  
21 from the clinical trials, we would hear from that, from  
22 meetings that we go to, and then we would be asking for  
23 either named-patient access or when licensing of those  
24 drugs took place.

25 Q. So was it not until the 1990s --



1 A. It would be early 1990s, yes.

2 Q. Would these drugs have been used individually at that  
3 time, rather than in combination with Zidovudine?

4 A. Unfortunately that would be the case. Remember again,  
5 over time if there was one drug available, you worked on  
6 that drug and the big debate sometimes was: did you add  
7 a second drug to the first drug or do you just switch to  
8 the new drug? And we were still learning about  
9 resistance.

10 We now know that there is cross-resistance within  
11 the same class of drug, ie all the three drugs you  
12 mentioned -- Zidovudine, Didanosine and Zalcitabine --  
13 they are all of the same class. So it is quite likely  
14 that if you have resistance in one drug, there is less  
15 efficacy in the other drugs as well. But nonetheless,  
16 we didn't know about resistance that much.  
17 Characterisation of resistance was very poor: only in  
18 the research lab. And access to resistance testing  
19 wasn't available anyway. So it was just doing what we  
20 felt was best for the patient.

21 Indeed, when we did change, there was some benefit  
22 but again that was short-lived. It was almost trying to  
23 buy time until better drugs became available.

24 Q. Right. So by the early 1990s, a patient may have been  
25 treated with Zidovudine or one of those two drugs we

1 spoke about on a named-patient basis?

2 A. Yes.

3 Q. But it would be still individual treatment rather than  
4 dual therapy?

5 A. It would be. I have occasionally used two drugs  
6 because, from my experience as an infectious disease  
7 doctor and experience of treating TB, for example,  
8 tuberculosis, we knew that if you use two drugs, you are  
9 probably making it more difficult for the organism to  
10 get resistance quickly.

11 So I was doing it even before guidelines came but it  
12 was tricky to do something outside the guidelines. You  
13 have to look at the evidence, you have to make sure that  
14 the benefits outweigh the risks. Because using two  
15 drugs meant potentially two sets of side effects and it  
16 was a tricky thing. And it was only until guidelines  
17 came that a lot more clinicians would be comfortable  
18 about using them in combination.

19 Q. What were the side effects of DDI and DDC? Were they  
20 similar to Zidovudine?

21 A. Different and similar in some ways. Didanosine had to  
22 be taken on an empty stomach. You had to be fasted.  
23 Then it can cause pancreatitis, which is inflammation of  
24 the pancreas, which can be quite debilitating and people  
25 have to fast when they have this condition. If you are

1 thin already from HIV/AIDS, you get thinner and  
2 obviously you are ill in hospital. It can also cause  
3 peripheral neuropathy, which is an inflammation of the  
4 nerves, which can cause very painful feet and hands.  
5 Not pleasant at all. There were issues about those  
6 drugs, it was trying to get the balance right.

7 Q. At page 7 of your report at the top, you tell us the  
8 point you have already made, that awareness came as to  
9 the limitations of using a single drug. That was in  
10 1989 in relation to a combination of two drugs in 1997.  
11 In the next paragraph you tell us that, as these drugs  
12 lost their efficacy because of drug resistance, patients  
13 became symptomatic and would develop further  
14 opportunistic infections. You go on to tell us about  
15 other treatments which were tried for patients with  
16 symptoms of AIDS. I presume you mean many clinicians  
17 there were desperate to try anything to keep them alive?

18 A. Both clinicians and patients as well. And, remember,  
19 they were very young people in those days and it was  
20 a death sentence, and the difficulty sometimes, and  
21 still now, is patients wanting some treatment which  
22 hasn't been found to be effective, and when faced with  
23 this situation, it's a balance of doing no harm and if  
24 it may do some good, why not try it. And again until  
25 guidelines came, it would be very difficult -- even if

1 guidelines were there -- and faced with a patient, it  
2 can be very difficult to not do anything. But sometimes  
3 it's dangerous to try and do something which may be  
4 harmful as well. It was a very difficult time for some  
5 clinicians in those days.

6 Q. You tell us there about intravenous immunoglobulin  
7 treatment and had that previously been widely used to  
8 treat idiopathic thrombocytopenic purpura. Can you tell  
9 us what that is?

10 A. This is a condition whereby your body attacks the bone  
11 marrow and there are less platelets available to stop  
12 bleeding in the circulation. Basically people have used  
13 steroids in the past, people have used splenectomy, to  
14 take the spleen out, but this is a sort of another way  
15 of treating this condition. It's also present in HIV as  
16 well, therefore there would have been experience among  
17 clinicians to use this modality and therefore it was  
18 felt to be safe enough to be tried even as a last resort  
19 for patients who had no other options available.

20 Q. Is that the same as thrombocytopenia?

21 A. Yes, they are the same, which is one way of naming that.

22 Q. So intravenous immunoglobulin treatment might have been  
23 used for patients who had thrombocytopenia as a symptom  
24 of HIV, but might it also have been used even if there  
25 was no thrombocytopenia?

1 A. Yes.

2 Q. Yes.

3 A. In certain conditions. I still use it in some of my  
4 patients who get recurrent pneumonia with HIV. The  
5 basis for that is there is a defect in antibody  
6 production in the subset of HIV positive patients and  
7 they can benefit from the use of this modality to  
8 prevent bacterial infections.

9 Q. Is that still used now?

10 A. No.

11 Q. No.

12 A. It is used for the conditions I have listed here but not  
13 for HIV treatment per se. It would be used for other  
14 things.

15 Q. You tell us in the next paragraph about --

16 THE CHAIRMAN: Could I ask a question before you pass on?

17 Professor Leen, you mentioned a short time ago that  
18 you have experience of patients coming and asking for  
19 drug therapy using preparations that have not yet been  
20 proved to be effective, and sometimes you would give in  
21 if it weren't going to do harm and so on. Was this  
22 right across the range of your patients or were there  
23 particular pressure groups that seemed to be better  
24 informed than others about emerging therapies?

25 A. I think all of them.

1 THE CHAIRMAN: All of them?

2 A. I mean, in the sense that -- it depends on how well-read  
3 you are, and obviously there is a lot of literature  
4 around for patients, a lot of support groups, and  
5 patients being desperate when they hear something, they  
6 want to try it. Very weird things they come up with  
7 sometimes. They have heard somebody has tried something  
8 and not published in the medical literature and they ask  
9 for it. But obviously I only accede to things which  
10 I feel comfortable with.

11 But there is a pressure and it's not only people in  
12 the late stage of the disease. Some patients even today  
13 want me to try things that are not in the mainstream of  
14 accepted treatment modalities just because they don't  
15 want to touch the HIV drugs, they just want to try  
16 something different and I would decline going down that  
17 line for those people who are reasonably well.

18 THE CHAIRMAN: But there are two aspects to it that I think  
19 interest me. One is to try to get a proper impression  
20 of the state of mind of the patient, and it's clear that  
21 there would be some very desperate people among those  
22 who come to you for treatment, and that's because of the  
23 perception of the mortality and morbidity associated  
24 with the disease.

25 A. True, yes.

1 THE CHAIRMAN: Then the other aspect is access to  
2 information independent of the clinician, because I do  
3 want to get a picture of where the initiatives are  
4 coming from, from time to time.

5 A. The weird, unusual modalities -- the weirder they are,  
6 the more likely they are coming from the bush telegraph,  
7 people talking to each other and hearing what's  
8 happening elsewhere in the world, in the USA. You are  
9 probably aware that even around that time there were  
10 AIDS denialists as well. Some people have postulated  
11 that AIDS is not due to HIV, it is due to some other  
12 condition and this is what you should try.

13 So you can see there are a lot of misconceptions  
14 about AIDS and HIV and some patients do feel that they  
15 want to buy into the alternative version of what's going  
16 on as well. And as clinicians we want to keep the  
17 dialogue open and try and work with the patient and  
18 hopefully bring them back to mainstream clinical  
19 practice, as opposed to being out on a limb doing  
20 something totally unethical.

21 THE CHAIRMAN: Is this an aspect of clinical medicine that's  
22 peculiar to HIV/AIDS or are there other infectious  
23 diseases, areas, where one might experience the same  
24 sort of interplay between the clinician and the patient?

25 A. There are quite a few of these.

1 THE CHAIRMAN: There are?

2 A. To name but two: management of chronic fatigue, patients  
3 have their own views sometimes from the clinicians;  
4 perception of whether Lyme Disease is a chronic  
5 condition or not. There are lots of areas where it's  
6 very grey, and in those areas the research might be  
7 probably less well defined than the AIDS/HIV area, and  
8 yet we still have a group of patients asking for some  
9 form of therapies which are less accepted.

10 THE CHAIRMAN: Thank you very much.

11 MS PATRICK: You mention there hydroxyurea and the fact that  
12 this was used for a while but was associated with  
13 significant toxicity. Was that used for a time in  
14 Scotland?

15 A. We have used it in Scotland as well. Quite often it's  
16 because we have been to a meeting whereby data on the  
17 use of this drug has shown it to have some  
18 effectiveness, and because of lack of other alternatives  
19 and hydroxyurea was a licensed drug already but not for  
20 HIV.

21 So there we can see clinicians using a licensed drug  
22 but for a different indication. And that's where some  
23 of the concerns arise as well and it creates a very  
24 significant clinical governance issue for the health  
25 trusts and the boards because it is not approved for use



1 in that area and yet it is being seen to be used in  
2 different conditions.

3 Q. It wasn't used but you could still use it? Did you have  
4 to justify that decision?

5 A. In those days we didn't have to justify it except  
6 amongst a group of ourselves, saying, "Yeah, we have  
7 seen data. It's worth a try because there is nothing  
8 else to use." But over the last five or ten years, it  
9 would be difficult to do that without filling in forms,  
10 getting it supported and approved by the directorate in  
11 the trust for use of those drugs. It is much tighter  
12 now, which is better for the patients.

13 Q. Yes. So were there any other treatments used in the mid  
14 to late 1980s and early 1990s in respect of symptoms of  
15 AIDS?

16 A. There were lots of other things tried. Some people have  
17 used steroids as a last ditch measure because it helps  
18 remove some of the symptoms. Again, it was almost like  
19 sort of totally uncharted territory. You could do  
20 almost whatever you wished to do if you convinced the  
21 patient, or at least you talk to the patient and say,  
22 "That's worth a try", and that's where the guidelines  
23 were crucial, to make sure that people were doing what  
24 was required.

25 But then again, it was easier to make the guidelines

1           then because there were drugs available. It was  
2           a totally different sort of face of HIV; the prognosis,  
3           what could be done, was much better. The prognosis had  
4           improved already by then. So in those days when there  
5           was nothing to offer, it was difficult, very difficult.

6   Q.   Yes. We know that patients were prescribed  
7           co-trimoxazole as prophylactic treatment to prevent PCP.  
8           When did that start?

9   A.   Quite early. I think as soon as we knew that PCP, which  
10          is pneumonia, was first diagnosed among the first AIDS  
11          patients in 1980/1981 -- we knew it recurred. And very  
12          soon we knew that we had to prevent it from recurring  
13          and that's why we started two things. Those patients  
14          who had PCP would definitely get (a), an antibiotic by  
15          mouth or by breathing it in, to ensure that the risks of  
16          recurring is less. And then, once we knew more about  
17          PCP, we were giving this antibiotic by mouth or by  
18          inhalation to people whose CD4 cell count was less than  
19          200. That's a marker of how depressed the immune system  
20          was and how likely it was going to start recurring.

21                 Also we were looking at how best to improve quality  
22          of life. Because if, let's say, we knew that the immune  
23          system was very weak, we could predict what type of  
24          opportunistic infections were likely to occur in some  
25          patients. Therefore, if you have nothing to give to

1 stop HIV and AIDS progression, you could prevent some of  
2 the infections which would impair the quality of life  
3 and also could be life-threatening.

4 So we were giving antivirals for some patients with  
5 recurrent herpes simplex, for example and, as it turns  
6 out now, we know that Acyclovir has some anti-HIV  
7 activity -- very little, but it was a little bit in  
8 there -- and sometimes we were thinking about giving  
9 other antivirals to prevent cytomegalovirus infection of  
10 the eye, for example, which was the cause of quite  
11 a debilitating condition, because it can lead to  
12 blindness. So it was not just trying to extend life, it  
13 was also to try and prevent likely severe conditions  
14 which would impair quality of life.

15 Q. And you touch there on looking at a patient's CD4 count.  
16 I think later on advice on using CD4 cell count and  
17 clinical assessment of a patient to monitor the disease  
18 progression was formulated. How were patients monitored  
19 in the 1980s? Did looking at the CD4 cell count come  
20 into play early on?

21 A. I think that way back in the mid 1980s we had access to  
22 this test. It's an expensive test but it was available  
23 and most centres, big enough centres, would have access  
24 to it. I remember, when I was in Manchester in 1986, we  
25 had the measurement of CD4 cell count. So that was much

1 earlier than any of the other tests that we could do and  
2 over time it is actually probably one of the best sort  
3 of measures that we have in terms of assessing the  
4 progression of the infection.

5 Q. Yes. And so the guidelines that exist now refer to  
6 those and recommend starting HIV treatment when the CD4  
7 count falls below a certain level and also where there  
8 are certain clinical symptoms?

9 A. True. I think anyone who has got symptoms which are  
10 related to HIV, so, whatever the CD4 count was, it  
11 probably wasn't functioning as well as somebody who has  
12 got the same levels of CD4 count. So numbers are  
13 one thing but, in terms of the immunological test, the  
14 function of CD4s is probably more technically demanding  
15 and not available on a clinical basis. So it would be  
16 a research tool, as opposed to a clinical tool. So, if  
17 you have got symptoms which we suspect may be  
18 HIV-related, then I think, whatever CD4 cell you are,  
19 you should be offered therapy.

20 The next question that arose is when you had no  
21 symptoms whatsoever and you got C4 counts. At what  
22 cut-off are we going to suggest using those drugs? The  
23 dilemma has always been the balance between toxicity,  
24 resistance, treatment fatigue versus the benefit over  
25 a long period of time.

1           So, as the drugs became more tolerable, easier to  
2           take as well, less toxic, and as we knew that there were  
3           more drugs in different classes being discovered and  
4           licensed, the balance started to shift and therefore the  
5           doctors were feeling more positive and therefore wanted  
6           to start treatment a bit earlier.

7           We also learned that if you start treatment late, ie  
8           with low CD4 cells, then the lower CD4 cell the patient  
9           has, that has a bearing on overall survival and in terms  
10          of the recovery of the CD4 cells when you start HIV.

11          So all these things were getting us thinking about  
12          where is the balance, and the pendulum swung every now  
13          and then. I think the Americans are much more gung ho  
14          than us, they are much more aggressive, and they are  
15          starting now with a CD4 count of less than 500, which is  
16          just slightly abnormal, whereas in the UK we are still  
17          starting at about 350 as the count.

18   THE CHAIRMAN: Professor Leen, there could be a danger at  
19          this point, I think, of assuming that the significance  
20          of a reducing CD4 count has always been understood. We  
21          know that in very early days in the study of this, 1981,  
22          1982, 1983, a reduction of CD4 counts, and indeed the  
23          balance CD4/CD8, were two of the biometrics that were  
24          reported. But the state of play that you have just  
25          outlined, is that the result of a long process of

1           developing knowledge?

2    A.   Oh, it is.  It certainly is.  It certainly is.  The  
3           prognosis -- and all this stuff is now available only  
4           recently -- in terms of how good the prognosis is.

5    THE CHAIRMAN:  For example, septrin was used very early on  
6           in trying to deal with PCP.

7    A.   And preventing it as well.

8    THE CHAIRMAN:  Yes.  Had it been fully trialed at the time  
9           that it was used first or was that experimental?

10   A.   The treatment for PCP?

11   THE CHAIRMAN:  For PCP.

12   A.   I think it probably was used because there was an  
13           experience using septrin in patients with PCP in other  
14           conditions.  Remember, PCP was not only in HIV patients.  
15           So when PCP was identified, obviously septrin was used  
16           in those patients.  Then again for this condition  
17           sometimes after a while there is resistance to septrin  
18           as well.

19   THE CHAIRMAN:  Yes.

20   A.   So other drugs had to be identified and used in that  
21           context.  But there was no clinical trial as such to  
22           show that; it was just from learning from what has  
23           happened in the past in other conditions whereby PCP was  
24           treated.

25   THE CHAIRMAN:  Professor James is suggesting to me that

1           there was a stage when, without full clinical trials,  
2           things were being done. One did know about reducing CD4  
3           counts but really there wasn't the very developed  
4           knowledge that you have been outlining recently.

5   A.   I agree.

6   THE CHAIRMAN:  And that happened just bit by bit.

7   A.   I agree, it is.  And unfortunately for me -- I was there  
8           from the start and knowing exactly the timeline is quite  
9           difficult.

10  THE CHAIRMAN:  I suppose it's difficult now to disentangle  
11           the points at which knowledge dawned on the route.

12  A.   It's difficult.  It's a gradual thing as well and from  
13           what you learned from going to a meeting, which is not  
14           published as a paper, to what eventually gets published,  
15           yes.  It's very difficult.

16  THE CHAIRMAN:  Yes, thank you very much.

17  MS PATRICK:  So how effective was treatment for HIV and AIDS  
18           in the late 1980s to the mid 1990s?

19  A.   Pretty poor actually.  It was still a death sentence,  
20           very much so.  Very much so.  Even using two drugs, out  
21           of guidelines, recommendations-type thing, it still did  
22           not hold the virus at bay.

23  Q.   So what was the prognosis for a patient who was  
24           diagnosed with HIV during that time?

25  A.   The figure was a median survival, 50 per cent survival,

1 two years at most, once AIDS is diagnosed, and as  
2 clinicians we would probably be watching the patients  
3 until they are symptomatic or drop their CD4 cells to  
4 a certain level, before we were going to offer treatment  
5 with one or two drugs.

6 Q. Okay. You have touched on this already but you tell us  
7 in your report, from page 8 onwards, about really the  
8 breakthrough in treatment for HIV coming in the  
9 mid-1990s. You tell us, firstly, at page 8 that one of  
10 the causes of this marked improvement was the arrival of  
11 a new class of drugs, the protease inhibitors. You have  
12 helpfully produced a table at page 12 of your report  
13 which, if you scroll down a little bit, shows at the top  
14 the year that individual HIV drugs were approved by the  
15 US Food and Drug Administration. How quickly did it  
16 follow that they were used in the UK?

17 A. I think all of them bar one has been approved for use in  
18 the UK as such. In the first -- the top page. So very  
19 soon afterwards usually, within months usually.

20 Q. So this is maybe a few months out of date but would be  
21 the same for the availability of treatment in the UK?

22 A. As well, yes. The only drug that hasn't been  
23 approved -- not because it hasn't been approved, it's  
24 because the company has not taken the drug forwards for  
25 approval in Europe.



1 Q. And which one is that?

2 A. That's Delavirdine. But we have patients on it still --

3 on a named patient still on that drug. That's the one

4 between the Nevirapine, Efavirenz in 1997.

5 Q. Yes. So we see there that the first protease inhibitor

6 was Saquinavir, followed by Ritonavir, and Saquinavir

7 was first used in 1995 and Ritonavir in 1996. When

8 these drugs were first used, were they used on their own

9 or were they used in combination with what already

10 existed?

11 A. It's a very good question. I think it was used in

12 combination with whatever was available. A lot of those

13 patients may have had those other drugs as monotherapy,

14 single drug, before, but nonetheless we just added that

15 in to make sure that we get as strong a regimen as

16 possible to suppress HIV.

17 Q. Yes. So you started to see improvement --

18 A. Yes.

19 Q. -- in treatment when you used these drugs in combination

20 with another one?

21 A. For those patients who are able to take three drugs

22 together from the start, the benefit was better and

23 lasted longer because if, let's say, you have had

24 exposure to some of the previous drugs, it is likely

25 that resistance has already occurred and they are not as

1           effective so therefore, even those drugs used as an  
2           add-on weren't as effective as if you were to use them  
3           as part of a three-drug version.

4   Q.   Yes.  You tell us further on in your report at page 17  
5           that the early drugs in the protease inhibitor class  
6           were associated with an increased tendency for increased  
7           bleeding times for people with haemophilia?

8   A.   Yes.

9   Q.   So if a patient came to you with haemophilia, would that  
10          have put you off using the protease inhibitors at that  
11          time or did you go ahead and use them and cover the  
12          patient with more factor?

13  A.   The decision about using protease inhibitors in  
14          a haemophiliac would be made in conjunction with the  
15          haemophilia doctors as well obviously, and the patient,  
16          and then what we would have done -- I remember one case  
17          I looked after, where there was no other option  
18          available for the patient, and the question is: should  
19          we use a protease inhibitor?  And if we did use the  
20          protease inhibitors, what can we do to minimise the risk  
21          in terms of bleeding?

22                 So that's how we would have done it and indeed, in  
23          this patient with the haemophilia doctors, we agreed  
24          that.  There is too much to lose by not trying it.  
25          "Let's try it and give more factors to compensate for

1 the bleeding time." That's what we did.

2 Q. Okay. The later protease inhibitors, did they have less  
3 of a side effect?

4 A. It's very difficult to know for sure. I have used one  
5 after discussing with my colleagues in London at the  
6 Royal Free -- they have got a big haemophilia cohort  
7 there -- and one of my patients needed one. So I asked  
8 the company, they gave me whatever they had at the time,  
9 (inaudible), the drug Kaletra, for example, and they  
10 said, "We don't know. There is a caution there." The  
11 haemophilia doctors in London said to me, "We have tried  
12 it, it seems to be okay." And then I tried it on the  
13 patient and it seemed to be fine. And I did find just  
14 recently, to see what else has been published in this  
15 area, and there was a case report of three patients  
16 from, I think, France, who had a prolonged bleeding  
17 time.

18 The difficulty about these things is you don't have  
19 a denominator: how many have been tried and how many  
20 have had this. So it's a case report with three cases.  
21 So it does exist but how common it is and how relevant  
22 it is in terms of the whole breadth of the haemophilia  
23 sort of expression of the disease is unclear. So it's  
24 something you would do in conjunction with the patient  
25 and the haemophilia doctors and learn how to manage

1           this.

2   Q.   So it didn't prevent patients with haemophilia being  
3       treated with these drugs generally?

4   A.   They would be worried but then obviously, when we make  
5       up a plan and explain the support we could give to  
6       minimise -- to stop it if there is an issue. But now,  
7       obviously we have got more than three classes of drugs,  
8       the pressure is less, we can use all the drug classes if  
9       we want to and get similar results.

10   Q.   Okay. So looking back at page 8, we were looking at the  
11       progress that is being made in the mid-1990s. You tell  
12       us there in 1996 that there were five large randomised  
13       clinical trials and they suggested that combination  
14       antiretroviral therapy was superior to nucleoside  
15       analogue monotherapy. At that point was that  
16       combination antiretroviral therapy with two drugs as  
17       opposed to three?

18   A.   There were some with two but there were some with three  
19       as well.

20   Q.   Right. If we could move down that page, please, you  
21       tell us at the bottom that some patients were so ill  
22       that the clinicians at the time thought they would not  
23       survive but the advent of these new drugs led to  
24       remarkable recovery and many of these patients are still  
25       alive today. So it was obviously quite a dramatic

1 change at that time in treatment for HIV?

2 A. It was an amazing time, completely changed the face of  
3 HIV and AIDS completely.

4 Q. Yes.

5 A. I have had patients who, you know, were getting married  
6 because they thought they were going to die. They got  
7 married in hospital because they can't deal with going  
8 anywhere else, and it would be to survive and, you know,  
9 some of them have got children and grandchildren now.  
10 It's amazing what this drug did to the whole HIV/AIDS.  
11 It was amazing. Really remarkable.

12 Q. Yes. Then you go --

13 THE CHAIRMAN: Ms Patrick, be conscious of the time.

14 I don't know whether the stenographer is happy to go on.  
15 I think if you stop now. The stenographer can't keep it  
16 up forever.

17 (11.15 am)

18 (Short break)

19 (11.38 am)

20 THE CHAIRMAN: Yes, Ms Patrick?

21 MS PATRICK: Just before the break, Professor Leen, we  
22 looked at page 8 of your statement and the five large  
23 randomised clinical trials. I was asking you whether it  
24 mentions combination antiretroviral therapy against  
25 nucleoside analogue monotherapy. I asked you if these

1 trials were in relation to two drugs or three. What's  
2 your answer in relation to that?

3 A. I think I may have said three but I was wrong. It was  
4 two drugs versus one drug.

5 Q. So at that time it was suggesting that you are better  
6 with two drugs as opposed to one.

7 At the very bottom of that page, you tell us about  
8 the start of the HAART era, the highly active  
9 antiretroviral treatment era. Can you explain what this  
10 was?

11 A. I think that was the recognition that taking three drugs  
12 was better than taking two drugs, which was better than  
13 taking one drug, and that's what changed the whole face  
14 of HIV.

15 Q. Did this show a marked and sustained clinical  
16 improvement in patients?

17 A. Yes, it did, for those people where those three drugs  
18 were active. So if you had drugs to which the virus was  
19 resistant, then it won't be triple, it will just be dual  
20 drugs. But sometimes you just used whatever was  
21 available.

22 Q. Yes. If we go over the page, you tell us that during  
23 these early ten years -- what early ten years are you  
24 referring to there?

25 A. From about 1985 to 1995, about those ten years, yes.

1 Q. You learned about drug resistance and how a combination  
2 at the end of the ten years of three drugs could prevent  
3 the emergence of HIV-drug resistance. You tell us of  
4 advances in HIV virology and virological tests, which  
5 enabled you to understand the dynamics of HIV  
6 replication. One of those tests was the HIV viral load  
7 test that was shown to be extremely useful to determine  
8 the efficacy of the drug treatment, and it became  
9 available in the clinic in August 1996.

10 A. It was in Edinburgh but I think not all centres would  
11 have had access to it and they may have had to send the  
12 blood elsewhere for it to be done.

13 Q. Is that what would have happened if you didn't in your  
14 own hospital have access to that test? Would you have  
15 sent it off to somewhere?

16 A. We would have, but luckily enough for us in Edinburgh,  
17 there was a big epidemic in Edinburgh, so we had access  
18 to the test very quickly.

19 Q. Then the guidelines in 1997 recommended that that viral  
20 load measurement should be made more widely available to  
21 physicians. So that would have flagged up to physicians  
22 then that this was something they should be taking  
23 account of?

24 A. And getting access to it for the patients, yes.

25 Q. You tell us that if the patient's viral load was

1 detectable while on treatment, then HIV-drug resistance  
2 was likely to emerge and if the viral load was  
3 undetectable, then a patient was at a much smaller risk  
4 of developing new opportunistic infections.

5 Further down that page you tell us about the HIV  
6 resistance test, which starts to become available in the  
7 clinic from 2000 onwards, and that was a test that  
8 allowed you to predict which HIV drugs were unlikely to  
9 be effective in your individual patients.

10 You tell us at page 10, under the heading "HIV drug  
11 concentration", that you became quickly aware that  
12 patients were all different from each other in terms of  
13 side effects they suffered, how the drugs were  
14 metabolised, how the drugs were absorbed or cleared from  
15 their body and how the drug/drug interactions affected  
16 the drug level in the patient's body. So presumably  
17 these new tests allowed the clinician to have a better  
18 picture of the effectiveness of treatment for that  
19 particular patient and then allowed the treatment to be  
20 tailored to suit that particular patient?

21 A. Indeed.

22 Q. You tell us at the bottom of page 10 that HIV can affect  
23 most organs of the body, and in the early years  
24 HIV-associated dementia and other significant  
25 neurological complications were serious and disabling



1 consequences of HIV. Was PML a consequence of HIV?

2 A. PML is a consequence of the immune deficiency caused by  
3 HIV. It's caused by a virus called JC virus.

4 Q. Yes. But you tell us there that in such cases it's  
5 important to ensure that HIV drugs could get into the  
6 brain in sufficient amounts so as to suppress HIV  
7 replication there. So these tests we discussed would  
8 help you ascertain that?

9 A. Yes and no. I think, first of all, having access to the  
10 blood tests that allowed measurement of drug  
11 concentration is only available in one place, and that's  
12 in Liverpool. So we can do it in the blood but we would  
13 infer from studies published to look at measurement of  
14 drug concentration in parts of the body. So we would  
15 infer from those studies that some drugs are better at  
16 getting to those areas than others, and we therefore  
17 choose those drugs if we are worried about HIV dementia  
18 and other things.

19 And indeed, what we have learned now is if there is  
20 pathology in the brain, like if you have an abscess, it  
21 is probably more likely that HIV will spill out in that  
22 area and cause problems as well. So now we know that  
23 when there is brain pathology we choose drugs which we  
24 know can have good penetration in these areas to prevent  
25 this complication. So they are all different. So we

1 choose those which are probably better at getting into  
2 that area.

3 Q. You tell us at page 11 that you now have around 30  
4 individual drugs from six drug classes to choose from  
5 when you are treating a patient, and there is obviously  
6 the guidelines which we have spoken about already. You  
7 say that you are now very good at managing your patients  
8 and there are only a small number of patients who have  
9 run out of treatment options. The majority of patients  
10 have fully suppressed HIV infection while taking  
11 treatment and those who are not controlling their virus  
12 have adherence issues, which I'm going to come on to  
13 shortly.

14 You tell us that there is no cure as the virus  
15 starts replicating when the drugs are stopped, but HIV  
16 can remain dormant in certain long-lived, latently  
17 infected memory cells in the body. So effectively it  
18 remains dormant while the antiretroviral therapy is  
19 being taken but as soon as that is stopped, the virus  
20 will reappear and will start replicating.

21 I would refer you now to page 13, where you talk  
22 about the efficacy of treatment for HIV and AIDS. You  
23 refer at the beginning to, I think what you mentioned  
24 earlier, that without treatment only 50 per cent of  
25 patients survive one year and only 20 per cent after

1 three years.

2 You tell us in the second paragraph that together  
3 with the increasing knowledge of HIV management, the  
4 availability of new drugs and new classes of HIV drugs,  
5 the prognosis began to progressively improve over time,  
6 as you have told us.

7 You tell us that the newer drugs are not only more  
8 effective but they are also more simple and more  
9 tolerable to patients. Is that just having to take them  
10 and how regular they are needed?

11 A. Yes, I mean, yes. In early days the treatment can be  
12 very complex. Some needed to be taken on an empty  
13 stomach, others better with food to aid absorption, the  
14 pill count was huge, remembering to take them when you  
15 feel unwell is not easy. And it's amazing now, there is  
16 now one formulation, which is one tablet, which contains  
17 three drugs, taken once a day and that's a complete  
18 change from taking about 20 to 30 pills in a day,  
19 amazing.

20 Q. It must be easier for the patient?

21 A. Very much easier.

22 Q. Over the page at page 14 you tell us about a recent  
23 study of a multinational collaboration of HIV cohort  
24 studies, showing the projected life expectancy of HIV  
25 infected/treated individuals who were 20 years of age,

1           increased from 36.1 years in 1996 to 1999, to 49.4 years  
2           in 2003/2005. You refer to another study from the  
3           Netherlands and tell us that the number of life years  
4           lost varied between 0.4 if diagnosed with HIV at age 25  
5           and 1.4 if diagnosed at age 55. For patients with  
6           HIV-related symptoms that range was 1.8 to eight years.

7           You tell us that currently most HIV physicians  
8           believe that with treatment, most HIV-infected patients  
9           will have a near normal lifespan. With near perfect  
10          adherence to HIV treatment, the virus is fully  
11          suppressed and over time this allows the immune system  
12          to recover and it may eventually return to normal.

13          If you scroll down, please, you tell us also that  
14          when HIV is fully suppressed by treatment, it's believed  
15          that the infectiousness of the patient is decreased  
16          significantly too and so this lowers the risk of  
17          transmission through sex or through blood contamination.

18          You tell us that now spontaneous vaginal delivery is  
19          now an acceptable clinical practice for mothers whose  
20          HIV load is undetectable whereas in the past, early  
21          clinical trials recommended Cesarean section.

22          We have touched on the importance of adhering to  
23          medication and I would like to now refer you to page 20  
24          of your report, where you tell us that non-adherence to  
25          prescribed treatment for HIV leads to the emergence of

1 drug resistance and subsequent failure of the anti-HIV  
2 regimen and immunological deterioration, and as you put  
3 it, patients become ill again.

4 You say that the drug resistance also means that  
5 other drugs in the same class may be less effective and  
6 this will limit future options for the patient. So if  
7 there is a problem with adherence to a drug in a class,  
8 that will not just affect the use of that drug but that  
9 class of drug in the future for effective treatment. Is  
10 that right?

11 A. Yes, it may well do.

12 Q. On page 6 of your statement you tell us that studies  
13 referred to show that 90 to 95 per cent of doses must be  
14 taken for optimal suppression and lesser degrees of  
15 adherence being associated with virological failure.

16 A. It would be with the older drugs as well and the figures  
17 might well be different with the newer drugs. One of  
18 the issues is that it depends how high the concentration  
19 of the drug is in the blood stream over a period of  
20 time. So if the levels drop down quickly, then the  
21 virus can reemerge and multiply. So the newer drugs now  
22 have a longer half-life. They stay in the body for  
23 longer and therefore they are more forgiving than the  
24 previous drugs provided you take it on the dot. That  
25 makes a big difference. So it may well be now that less

1 strict adherence might be required nowadays compared to  
2 what the drugs were in the early days.

3 Q. But in the early days you think that 90 to 95 per cent  
4 would have been --

5 A. Definitely.

6 THE CHAIRMAN: Over what period of time would the 90 to  
7 95 per cent be measured, Professor Leen?

8 A. It would be studies over a fixed period of time.  
9 I guess it would fit in with the levels in the blood.

10 THE CHAIRMAN: Yes. It just strikes me that 90 to  
11 95 per cent is so high that if the reference period were  
12 short enough, the patient couldn't miss a single pill.

13 A. It would be high enough to allow changes to occur as  
14 well. It's surprising sometimes. Sometimes my patients  
15 come to see me, they say they have stopped the  
16 medication on their own and yet the viral load is fully  
17 suppressed a week or so after. It just shows you how  
18 different the drugs are in terms of how the half-life  
19 is, how the patients handle it. But in those days that  
20 was the degree of adherence that was required and it  
21 would have been over a period of months, looking at  
22 that.

23 There are ways of doing it. They have electronic  
24 timers which will allow the researcher to know when the  
25 pill box was opened. It doesn't tell you if it was

1           taken -- when it was opened.  It's very difficult  
2           because asking patients about adherence is difficult  
3           because they will tell you what you want to hear:  
4           "I have taken everything."  So there are ways of doing  
5           it and sometimes it's asking the patients how many they  
6           have missed in the previous week, in the previous month.

7  THE CHAIRMAN:  If the half-life is increasing beyond the  
8           period between doses, what is happening?  Is there  
9           a cumulative protection building up that means it  
10          extends further or is it still the half-life of the last  
11          dose that determines things?

12  A.  I think it is probably -- it is so long that you can  
13          miss -- there was a study that was done, for example,  
14          whereby you take pills for five days and take a few days  
15          off and if the half-life is suitable, you can maintain  
16          suppression still.  So already you are talking about  
17          adherence for five out of seven days.  So those figures  
18          don't exactly work for every pill count but in the early  
19          years, when you had to take them two or three times  
20          a day, that was crucial.

21  THE CHAIRMAN:  It was crucial.

22  MS PATRICK:  At page 19 of your report you tell us about the  
23          difficulties for patients taking such treatments, and  
24          you tell us that when Zidovudine was first used in 1987,  
25          it was recommended that the patient took the medication

1 at four hourly intervals and you refer to the side  
2 effects, which you have already told us about. So you  
3 tell us that this meant that patients had to use timers  
4 to wake themselves up during the night to take the  
5 medication and so this had a knock-on effect in terms of  
6 tiredness and also must have caused some anxiety about  
7 being able to continue to do so and to remember to do  
8 so.

9 A. It's also interesting that later on we have learned that  
10 it is not the blood levels that matter, it's the level  
11 of the drug in the cell. Not that we use the drug now  
12 but when we were using it about ten years ago, we were  
13 using it twice a day. So as knowledge improved, we were  
14 able to help making sure that we don't create more  
15 anxiety in the patient by insisting on such rigid timing  
16 of the medication.

17 Q. Yes. But that was what you knew at that time and so  
18 that was what was done at that time.

19 A. Yes, exactly.

20 Q. You tell us that some treatments are taken twice a day  
21 and the interval between doses should be around 12 hours  
22 plus or minus one hour. Some treatments, as you have  
23 already told us, are best taken with food and others on  
24 an empty stomach to maximise drug absorption. Sometimes  
25 your cocktail -- as you have called it -- of



1 antiretroviral treatment may contain some drugs that  
2 need to be taken at both these times, which is very  
3 cumbersome for a patient and another hurdle for good  
4 adherence to the treatment.

5 If we scroll down, please, you tell us that around  
6 the mid-1990s -- was this your own personal  
7 experience? -- you had frequent complaints from patients  
8 about the number of tablets they had to swallow and the  
9 large size of them. And also there was the problem with  
10 the side effects of the treatment, which you have also  
11 told us about and I'll come on to shortly.

12 If someone had difficulty swallowing a tablet, were  
13 they able to crush it or dissolve it in water?

14 A. Yes, we would have to ask -- usually there are some of  
15 these pills. We had special crushers as well. One drug  
16 was Nelfinavir. It was very tough to take. It was blue  
17 as well. So that can be crushed, but we have to request  
18 evidence from the manufacturers that the bioviability is  
19 still the same. Sometimes you can't crush them.

20 There is a new drug, Kaletra tablet. We can't crush  
21 them. Apparently the shape of the levels in the body is  
22 not the same. So we have to ask them. If this is  
23 possible, we do it. Sometimes we can ask them to just  
24 dissolve it but then it's all the hassle about  
25 dissolving it and then the taste of it as well. Those

1           days were very difficult. We had to be creative and  
2           just try and solve the problems for the patients.

3    Q. For each individual patient, presumably. We will come  
4           on to the side effects, but you note there that taking  
5           the medication reminds patients that they have HIV  
6           infection and that too puts them off taking the  
7           treatment. As you have already said, remembering to  
8           take it at the required times is difficult, particularly  
9           if a patient does not have any symptoms, and sometimes  
10          patients have treatment fatigue. You tell us that  
11          also -- if we go over the page -- patients are  
12          understandably frightened about missing their medication  
13          because of the risk to them of HIV-drug resistance, if  
14          they do so.

15                 Also we have heard from witnesses about their wish  
16          to keep their HIV status to themselves and for people  
17          not to find out about that and you tell us that this  
18          causes difficulties too if somebody is at work or at  
19          school and needs to take their treatment at the set  
20          times, and some of these medications also needed to be  
21          stored in a fridge, which may be hard at work.

22    A. It may not be so for a short period of time but in the  
23          home, if you are sharing a flat with other people, if it  
24          needs to be kept stored in a fridge for more than a day,  
25          you have to hide it and you miss taking the medication

1           because you are hiding it.

2   Q.   You tell us also that patients may be prescribed  
3       additional medication to counteract side effects which  
4       just adds to the pill burden, as you call it, there.  
5       They include anti-sickness medication, anti-diarrhoeal  
6       agents like Immodium, and painkillers for headaches.

7           Could I refer you, please, to page 15, where you  
8       discuss the side effects of the treatment. Is it fair  
9       to say that the earlier drugs were associated with more  
10      side effects than the more recent drugs?

11   A.   Very much so. Unfortunately, again because there was so  
12      little available, option-wise, you had to stick to them  
13      or face inevitable progression of the disease. Tough  
14      choices, very tough.

15   Q.   Yes. You say earlier drugs were associated with many  
16      side effects affecting many organs and the side effects  
17      of the earlier drugs include headache, nausea, vomiting,  
18      diarrhoea, flatulence, skin rashes, liver inflammation,  
19      kidney stones, dysphoria -- what's dysphoria?

20   A.   Changing mood.

21   Q.   Weird and sometimes frightening dreams, depressive  
22      symptoms, tiredness, poor sleep and body shape changes.  
23      You tell us that sometimes if the side effects were  
24      significant, a patient would miss a pill and then the  
25      physician would have to change the treatment the patient

1 was taking.

2 Why did the treatment cause weird or frightening  
3 dreams?

4 A. I think any medication is associated with some sort of  
5 side effects. Unfortunately, it's one of those things,  
6 and there were so few drugs that whatever was different  
7 from the previous one -- it may be different because of  
8 being once a day as opposed to twice or a few times  
9 a day, it may be because it's a different class of  
10 drugs, because you need that to circumvent resistance  
11 issues -- it's one of the side effects. And  
12 unfortunately, when you don't have any option, you have  
13 to try and even license those drugs when they are  
14 intolerable.

15 But eventually the users would decide they won't use  
16 that drug because it's too intolerable. So needs must  
17 in those days and not everyone has those side effects.  
18 That's the thing. If, let's say, everyone had the side  
19 effects, then obviously there is no way this drug would  
20 be approved for use but there is a small group of  
21 patients who get those side effects.

22 Q. Would that interrupt sleep sometimes?

23 A. Oh, they would, they would, yes.

24 Q. You tell us in the second paragraph, and I think this is  
25 a side effect mostly of Zidovudine, the body shape

1 changes. Is that right?

2 A. There are two types of body shape changes and sometimes  
3 both types co-exist in the same patient. So there  
4 is the fat loss, which is caused by a class of drugs,  
5 the Thymidine analogues, that would be Zidovudine and  
6 Stavudine. Basically you lose fat around your face, you  
7 are very skinny and your arms and your veins are very  
8 prominent, your legs are also very thin and the buttocks  
9 as well. The fat can go and you look quite misshapen.  
10 And the worst of it is it reminds people of what AIDS  
11 patients used to look like in the early days, very thin,  
12 with no fat. So that's quite disturbing.

13 The other one is fat accumulation. You get the fat  
14 around the belly. So women who used to be very slim  
15 could have a very big, beer belly type thing, and that  
16 fat is unfortunately not in the skin. It's inside the  
17 body, it's inside the cavity. So you can't get at it.  
18 And that's associated also sometimes with a bit of a fat  
19 lump at the back, sort of thing.

20 So the worst is that you get these very skinny arms  
21 and legs and face and yet the fat in the tummy and in  
22 the back as well, and that's very troublesome to treat,  
23 very troublesome.

24 Q. Do some patients receive surgery for that?

25 A. Yes, what we have done is we can use fillers for the

1 cheeks or use a bit of fat transplant from the belly and  
2 put it in there to make this look better, but obviously  
3 we have to stop the drugs which cause that in the first  
4 place.

5 Q. Yes.

6 A. So we would do that. The trouble about the buttocks is  
7 that it's an area whereby it's not very clean because of  
8 where it is. Infection is a risk. If we put anything  
9 like that. So my plastic surgeon colleague will not do  
10 any restorative surgery around the buttocks. It's too  
11 risky, the risk of infection. In some cultures now big  
12 buttocks is something which is favoured and it can be  
13 very distressing for those patients from those cultures.

14 The fat around the back can be sucked out but if  
15 it's inside the belly, around the intestines, it's not  
16 possible to suck it out at all. And there is a drug  
17 licensed in the US which is growth hormone which can be  
18 used to try and reduce that fat. It's very expensive  
19 and it has got toxicity as well. But it hasn't been  
20 licensed, partly because they haven't requested  
21 a licence for it in Europe.

22 Q. Okay. So having heard about the importance of adherence  
23 to medication, you tell us that nowadays it is  
24 understood how important adherence to medication is and  
25 so patients receive adherence support from a number of

1 people, I think, when they attend an HIV clinic,  
2 including a clinical nurse specialist, a dietician,  
3 their doctor and maybe a counsellor. You tell us in  
4 your report that that was built into your unit in  
5 Edinburgh in about 1996 or 1997 and in 2001 the British  
6 HIV Association issued guideline about this.

7 What adherence support did patients receive in the  
8 1980s and early 1990s?

9 A. Very little. It's a bit like you get a prescription,  
10 take as much as you can and unless of course you start  
11 sitting with the patient and exploring how they are  
12 tolerating it, how much they are missing it, it wasn't  
13 going to work.

14 Q. No. Obviously we have heard that the side effects were  
15 worse of the early medication. So how did this affect  
16 patients' adherence to medication in that timeframe?

17 A. We were not asking about this. We probably didn't know.  
18 I'm sure it wasn't very good.

19 Q. I mean, presumably now, it is acknowledged that certain  
20 classes of people may need more assistance with  
21 adherence to treatment than others and I'm wondering  
22 here about teenagers, teenage boys. What would you say  
23 about that?

24 A. I'm not an expert but I do see them coming to my clinic,  
25 after they have survived their teenage-hood. They come

1 up to me with a very resistant HIV usually, because they  
2 have been fighting with the parents, getting them to  
3 take the medication, and it has been impossible to get  
4 as good an adherence as what we wanted, and they luckily  
5 enough when they come to me now, I have enough new drugs  
6 that I can use for them to circumvent those resistance  
7 issues.

8 I used to do a clinic with the paediatrician in  
9 Edinburgh just to try and help support best use of  
10 antivirals. Quite often they put PEG tubes, they put  
11 a tube in the stomach whereby the parents can just  
12 inject liquid drugs into their dosage. Even then  
13 sometimes it is very difficult to get the level of  
14 adherence that you need because children are children,  
15 there is always stress and they argue back, teenagers.

16 So it's very difficult and amazing how resilient  
17 they are despite all their resistance, that they are  
18 still surviving through their teenage years to come to  
19 the adult clinics. But it is a difficult job, a very  
20 difficult job for children.

21 Q. Thank you.

22 At page 16 of your report you tell us about risks  
23 associated with HIV treatment and you tell us that it's  
24 associated with an increased risk of cardiovascular  
25 disease, particularly among patients taking protease



1 inhibitors. What is that risk?

2 A. It is about 70 per cent additional to the same group of  
3 patients for age and lifestyle. Every year 70 per cent.

4 Q. You tell us that metabolic changes are also seen in  
5 patients taking antiretroviral treatment and these  
6 include diabetes mellitus, raised levels of lactic acid,  
7 raised cholesterol and triglycerides. You tell us that  
8 it's also associated with raised levels of liver  
9 enzymes. You tell us that there is an increased risk of  
10 fractures among HIV positive patients. Why is that?

11 A. That is very interesting. I think it is multifactorial.  
12 A lot of our patients probably do not exercise as much  
13 as others because they have been unwell or if they have  
14 lost a lot of weight. There is now talk about  
15 inflammation as a factor of how it affects bone  
16 formation, and bone is a very active thing. There is  
17 the deposition and also reabsorption all the time going  
18 on, and we are still learning a lot about what is really  
19 going on. Is it just the HIV itself or is it the drugs  
20 that we are giving them? And the balance of the  
21 inflammatory markers can be measured as well. We know  
22 there are changes when we start treatment with antiviral  
23 therapy as well. One of the drugs can cause sort of  
24 a reduction in the density of the bone as well. So it's  
25 a multifactorial thing and also sometimes patients have

1 a low level of vitamin D. It's complex and we are still  
2 trying to sort out what exactly is going on. But there  
3 is an increased risk of fractures in our patients.

4 Q. Given that it's a relatively recent treatment,  
5 presumably the long-term effects of it are going to take  
6 a while to come through?

7 A. Definitely, and not even that -- even if we do find  
8 things, we need to try and find which modality is best  
9 to try and reverse those changes or prevent those  
10 changes. So it will take some time, yes.

11 Q. Yes. Could I refer you to the next page and to the  
12 effect of a patient having Hepatitis C as well as HIV.  
13 You tell us that the Hepatitis C virus may have  
14 a deleterious effect on HIV progression. When you say  
15 "may" there, is that not --

16 A. Entirely agreed by everyone. There is a signal and as  
17 usual it is ascribing that to the cause. In a lot of  
18 the studies, it is not clear when each of the two  
19 infections were acquired and therefore to look at the  
20 influence of one against the other, it can be quite  
21 tricky.

22 Also the risk groups as well. I mean, in terms of  
23 the risk group, those who have both Hep C and HIV in  
24 early years were drug users and haemophiliacs. And drug  
25 users, when you study them as a group they have other

1 compounders, they have lifestyle, adherence to drugs.  
2 So it's very dirty and very difficult to do very good  
3 studies now for these things. But there is a signal  
4 that it may make it worse.

5 Q. You tell us there that some studies have demonstrated  
6 that infection with the Hepatitis C virus was  
7 independently associated with an increased risk of  
8 progression to AIDS or death, despite a similar use of  
9 antiretroviral therapies in the co-infected group  
10 compared with the group infected with the HIV alone. So  
11 would that take account of how effective the therapy is  
12 being?

13 A. Possibly. The other possibility is it may well be that  
14 those who are co-infected with Hepatitis C as well have  
15 more difficulties in terms of side effects with handling  
16 the HIV drugs as well, because a lot of the drugs do  
17 cause liver inflammation on its own anyway. And  
18 sometimes people want to reduce the dose and sometimes  
19 the level of the drugs are much higher because the liver  
20 doesn't metabolise them. So you are having extra levels  
21 of the HIV drugs as well.

22 Q. Okay. You refer there to a Swiss study which suggested  
23 that those patients with a dual infection may be less  
24 likely to achieve a CD4 count rise of at least 50 cells  
25 per millimetre cubed within one year of starting HAART

1 than those with mono-infection, but the viral load  
2 response to therapy was similar.

3 Then below that you talk about the effect of HIV on  
4 the Hepatitis C virus and tell us that evidence suggests  
5 that in an HIV positive individual, progression to  
6 cirrhosis is likely to occur more frequently and at  
7 a faster rate than in an immuno-competent individual.

8 Is that the case even if the viral load is suppressed?

9 A. We think that if the HIV virus is fully suppressed and  
10 if the CD4 cell count does go up, certainly above 200,  
11 the rate is probably about the same as those who are not  
12 co-infected but you have to have both.

13 Q. Yes. You tell us that Hepatitis C infection is now one  
14 of the major causes of death in people with HIV?

15 A. Who are co-infected --

16 Q. Who are co-infected. If you have a co-infected patient,  
17 how would you determine the treatment of that patient?

18 A. It will depend on which of the two viruses need  
19 addressing first, and that would depend on the state of  
20 the liver and also the HIV state as well. Having said  
21 that, if you treat the HIV, you are probably more likely  
22 to treat the Hepatitis C successfully than if the HIV is  
23 untreated, particularly if the CD4 cell count is a bit  
24 on the low side. Okay?

25 So it's a discussion. And interesting as well. If

1 your Hepatitis C is treated before you get HIV  
2 treatment, the changes in liver inflammation is much  
3 less, so it makes it more tolerable. So it's a dilemma.

4 The response rate of Hepatitis C treatment in the  
5 HIV-infected patient is lower. So it will depend on  
6 what's going on, and sometimes we will treat the HIV  
7 first, if they need HIV treatment. And then as soon as  
8 we can, we will start Hepatitis C treatment. If the  
9 patient agrees to it.

10 There are six types of Hepatitis C and there is one  
11 type in particular which is more difficult to treat.  
12 That's the type 1. In an HIV positive patients with  
13 a high viral load of Hepatitis C, which is about, let's  
14 say, 800,000 copies, the response rate is about  
15 17 per cent. So less than one in five. So not many  
16 patients would say, "I want to go for it". Very few  
17 would want to go for it. But if they are genotype 3,  
18 the response is about 60 per cent. So they are probably  
19 more likely to go for it.

20 So it's a balance. Most patients say they will do  
21 the HIV first and then worry about the Hep C. If some  
22 of them come with a good CD4 count, let's say 500, we  
23 will probably treat the Hepatitis C first because they  
24 don't need HIV treatment. That's the guidelines but in  
25 five years it probably might change.

1 Q. So the patient with genotype 1, who has that low chance  
2 of the treatment for the Hepatitis C virus being  
3 successful, and he chooses, understandably, not to take  
4 treatment, he is more likely to progress faster --

5 A. Liver-wise.

6 Q. Liver-wise, to cirrhosis?

7 A. Yes.

8 Q. You tell us over the page, at page 18, also that all  
9 antiretroviral drugs -- this is further down -- have the  
10 potential to cause acute and long-term hepatotoxicity  
11 and this risk is increased two to threefold in the  
12 presence of chronic liver disease, such as that caused  
13 by Hepatitis B or Hepatitis C.

14 So they are very intertwined and presumably each  
15 patient has to be looked at, as you say, depending on  
16 their condition in respect of the HIV virus and in  
17 relation to the Hepatitis C virus.

18 You tell us further up, in the second paragraph,  
19 that several studies show that liver related mortality  
20 rates are higher in those with a low CD4 cell count  
21 irrespective of the antiretroviral treatment use. So is  
22 that also irrespective of the viral suppression?

23 A. Yes, it would be.

24 Q. Yes. You say that there is some evidence that  
25 demonstrates a better outcome for the co-infected

1 patients with suppressed HIV infection compared to those  
2 with poorer HIV control. Guidelines have suggested  
3 starting HIV treatment for those co-infected with the  
4 Hepatitis C virus at an earlier CD4 cell count compared  
5 to those simply infected with HIV.

6 There are some specific guidelines for the  
7 management of co-infection with HIV and Hepatitis B or  
8 C, and I don't propose to refer to these but for  
9 reference these are [\[PEN0121100\]](#). You tell us that  
10 hepatocellular carcinoma is estimated to occur at a rate  
11 of 1 to 4 per cent per annum in patients with  
12 Hepatitis C virus-related cirrhosis. In patients who  
13 have HIV infection it tends to occur at a younger age  
14 and within a shorter time period. Does that depend on  
15 the CD4 cell count?

16 A. Obviously the lower the CD4 cell count, the more likely  
17 and faster -- the answer is probably yes, but the actual  
18 evidence probably concords with that but intuitively  
19 that's what would be likely to be the case.

20 Q. As you have already pointed out, you state there that  
21 the response to the Hepatitis C treatment with the  
22 current standard of care, pegylated interferon and  
23 ribavirin, is impaired in the co-infected patient  
24 compared to the mono-infected patients, and this has led  
25 many patients to defer treatment until better treatment

1 options become available.

2 Is that looking like some time soon?

3 A. There are, as we speak, two new drugs that would be used  
4 in addition to the current standard of care, that have  
5 been licensed in the US. Both of them are being  
6 reviewed by the European Medicines Agency and I think it  
7 would be licensed. Unfortunately, there is still a lot  
8 of research that needs to be done to look at drug  
9 interactions between the HIV drugs and the Hepatitis C  
10 drugs. So just now there have only been about 60  
11 patients worldwide who have been dosed with one of the  
12 two new drugs in HIV -- infected patients, and obviously  
13 we do need those drugs for this group of patients  
14 because the response rate is so poor otherwise.

15 THE CHAIRMAN: Professor, I wonder if I could ask a little  
16 about this topic?

17 These are very powerful new drugs clearly that are  
18 coming on to the market, and the drug you have just  
19 mentioned, is it undergoing clinical trials of these 60  
20 people or are we past that stage?

21 A. No, they are clinical trials and there are only two  
22 regimens that are allowed because they have done the  
23 drug interactions for those ones and you have to be able  
24 to go to use those antiviral drugs for HIV to be able to  
25 get to that study. So that is done in the US and Europe



1 and not in the UK, and it's too early yet to know how  
2 successful that will be. No doubt it will increase the  
3 success rate but how much we don't know.

4 THE CHAIRMAN: So it's an aspect of success that interests  
5 me. These very powerful new regimes, do any of them  
6 carry the potential for new risks to emerge in the  
7 future that are unanticipated?

8 A. Oh, yes. First of all, they are powerful but not that  
9 powerful to prevent resistance to these drugs. So what  
10 we are learning now is how best to use those drugs to  
11 allow future options to the new classes coming later if  
12 it doesn't work. So we are trying to identify the  
13 likelihood of response rate in those patients. They  
14 have side effects; they have rashes, anemia. But  
15 otherwise, if we can choose the right patient, we could  
16 minimise the risks in terms of resistance long-term.

17 THE CHAIRMAN: But what about the risk of new forms of  
18 pathology emerging in the future from the drug therapy  
19 itself?

20 A. Well, like anything that we have, only time can tell us  
21 about long-term safety. Okay? But the rationale behind  
22 the Hepatitis C pathology is that if you get rid of it,  
23 a lot of the changes do regress, and some of the  
24 patients which have had cirrhosis in the biopsy before,  
25 apparently the amount of scarring is much less after

1 a successful cure of Hepatitis C.

2 So you are right. I mean, we have to be vigilant in  
3 the long-term about using all these new drugs but it  
4 is directly acting on the virus itself, as opposed to  
5 modulating the immune system in order to get rid of the  
6 Hepatitis C.

7 THE CHAIRMAN: I can see the focus for improving the drug  
8 therapy, but of course, it would be rather a sad outcome  
9 for the infected patients if what has happened in the  
10 past were to recur and the new therapy generated its own  
11 adverse consequences down the line.

12 A. I agree, I agree with you. And this is why, for  
13 clinicians, it's a decision as to whether to jump and  
14 start treating everyone with that or treat those people  
15 with most needs, ie those who are quite advanced in  
16 terms of liver disease. But then again, those with  
17 advanced liver disease are likely to respond less well  
18 than those who are earlier. So as usual there is this  
19 quandary about when is the best time to use those drugs,  
20 and the good thing about Hepatitis C now is that a lot  
21 of lessons can be learned in terms of what we know about  
22 HIV in terms of virology and resistance. So there are  
23 some positive things but I agree entirely with you that  
24 they are not exactly known and long-term safety is  
25 something that we cannot say we have.

1 THE CHAIRMAN: There is going to be a continuing element of  
2 the unpredictable in all of the work you do.

3 A. Unfortunately so; yes.

4 THE CHAIRMAN: Yes, Ms Patrick?

5 MS PATRICK: I would just like to take you back once again  
6 to the early 1980s. You told us that patients did  
7 receive treatment for opportunistic infections as and  
8 when they occurred. Did that work for a time for these  
9 individuals?

10 A. It works for a time until the immune system is so  
11 battered they really can't do anything. Whatever you  
12 do, you are just delaying the inevitable.

13 Q. Yes.

14 A. So that's what did happen, yes.

15 Q. An example being that patients acquired PCP and septrin  
16 was able to treat this, maybe the first time, maybe the  
17 second but, as time went on, not so effective?

18 A. Exactly. Even now we have technology to predict if we  
19 have found the actual pathogen for the pneumocystis.  
20 There are tests that will look at resistance as well.  
21 So there are gene tests to see if septrin will work or  
22 not. So the technology is there. It is not easily  
23 available but it can be done. But luckily enough we  
24 have alternative drugs and sometimes people are so ill  
25 that despite being on a ventilator, it is not enough.

1 Q. Okay. Finally I would like to refer you to page 21 of  
2 your report, where you say at the top that HIV has  
3 a huge physical and psychosocial impact on HIV infected  
4 individuals and their families, and that the stress of  
5 living with HIV causes some people to suffer from mental  
6 health problems such as anxiety and depression. Is this  
7 what you have seen as a treating clinician?

8 A. Definitely. I think this is an underestimated problem.  
9 Unless of course you start asking direct questions and  
10 teasing it out, a lot of patients don't want to bother  
11 you. We are fortunate enough in this field to provide  
12 support for those who are affected with HIV, not only  
13 those who are infected, and unfortunately again the team  
14 of counsellors we have, that has been driven down  
15 because of financial reasons and what not. But this is  
16 a significant issue and more could be done, even today.

17 Q. Yes. Further down that page you refer to stigma and  
18 discrimination. Does that still exist in relation to  
19 the HIV virus?

20 A. Unfortunately very much. Very much. Unfortunately.  
21 I think the patient probably perceives that as being  
22 worse than what we think sometimes it may be, but it  
23 does exist, it does exist.

24 Q. I have no further questions. Thank you very much.

25 THE CHAIRMAN: Mr Di Rollo, do you have any questions for

1 the professor?

2 Questions by MR DI ROLLO

3 MR DI ROLLO: There are one or two questions that have  
4 occurred in the course of the evidence but there are  
5 also one or two questions that perhaps we would like the  
6 opportunity --

7 THE CHAIRMAN: I can't hear what you are saying.

8 MR DI ROLLO: Sorry. I think I'm on now.

9 Professor, one thing I would like to ask you is,  
10 between 1985 and 1990 or the early period, if someone  
11 was unaware of their diagnosis, that they were HIV  
12 positive, that would presumably mean they wouldn't get  
13 any treatment or treatment would be delayed. Would that  
14 have any effect or impact on the outcome for them at the  
15 end of the day?

16 A. It would all depend on the stage of their HIV at the  
17 time, and obviously if, let's say, they were ill with  
18 one of those AIDS-defining conditions, the answer is  
19 definitely yes because they would not be able to access  
20 the drug for HIV.

21 But if, let's say, they had a good CD4 cell count,  
22 they were asymptomatic, then no intervention would  
23 probably be offered anyway because they are well. So it  
24 all depends on their CD4 cell count and what symptoms  
25 they had.

1 Q. Right. Another point arising from that is that you  
2 indicated that patients were treated by the physician  
3 that diagnosed them in the initial period of time.  
4 Between 1985 and 1990 and perhaps later on but just  
5 sticking with that period, would it have been better if  
6 those patients had been treated not by the physician  
7 that diagnosed them but by a specialist or more  
8 specialist units?

9 A. It's a very tricky one because the speciality didn't  
10 quite exist, and as I said earlier, it all depends where  
11 you were. So, for example, in London Professor Gazzard,  
12 who is a gastroenterologist, he decided that he would  
13 take it on and he has one of the biggest centres in the  
14 country, and he is actually the founding chair of the  
15 association I'm part of. And even in London, if you  
16 had, let's say, a problem with your chest, like PCP, you  
17 may well have landed up with Professor Johnson, who is  
18 a respiratory physician, and she too is an excellent HIV  
19 treater.

20 So it depends not so much on the speciality that you  
21 landed in, it's more on the nature of the physician and  
22 the setup that the physician is in. If he has an  
23 interest in that area, then obviously it doesn't matter  
24 what was the name of the ology that you had but you are  
25 interested enough to learn about it, interested to care

1 for your patient and provide the best for him. That's  
2 what happened. But unfortunately it's touch and go  
3 depending on which part of the country you are in.

4 Q. Are you able to help us with, say, the central belt of  
5 Scotland, what the situation would be there?

6 A. I didn't come here until 1989 and in 1989 it would have  
7 been both GU doctors and ID doctors who were doing the  
8 work. Nowadays there is no such thing as a speciality  
9 of training for HIV, it is just either GU doctors or ID  
10 doctors. I really can't come out on that really.  
11 I would have hoped that anyone who looks after anybody  
12 with HIV knew their limits and asked for help from  
13 people that are knowledgeable about this.

14 Q. And where would the source of that help be at that  
15 particular time?

16 A. I think Edinburgh would have been a big centre and  
17 Glasgow as well.

18 Q. In Edinburgh where would you go, do you know?

19 A. I would say that the infectious diseases unit would be  
20 the biggest one; the one where I work.

21 Q. That would be at the City Hospital?

22 A. The City Hospital. In Glasgow it would be the  
23 Ruchill Hospital at the time, the infectious disease  
24 doctors. There's one in Glasgow. In Dundee there is an  
25 ID unit there. My recollection is that in 1989 there

1 would have been a new consultant in ID, who took a post  
2 in Dundee, King's Cross, or Ninewells at the time. But  
3 he probably was single-handed then, okay?

4 Q. Right.

5 A. Then basically people are learning and sometimes people  
6 hang on to the patient because they want to learn and  
7 increase their interest. It was, I'm sure, a very  
8 difficult time for patients. It is almost like the luck  
9 of the draw where you ended up in and what sort of care  
10 you received.

11 Q. Can I ask you one more thing. You mentioned  
12 co-infection. There is one question I would like to ask  
13 about that. You were dealing with the effects of  
14 co-infection. I'm not sure whether I fully understood  
15 whether or not you told us what the likely effect is if  
16 you defer Hepatitis C treatment, what effect would that  
17 have on a co-infected patient if that is deferred?

18 A. Well, the Hepatitis C virus, if it's still replicating,  
19 and we know that by looking at the virus in the blood,  
20 that would mean that the liver damage is ongoing and  
21 progressive and the next step would be cirrhosis, and  
22 then you get end-stage liver disease with all the  
23 complications of liver failure: bleeding from the  
24 varices and then the ascites, the fluid in your belly,  
25 cancer we mentioned, and what then would be a transplant



1 of the liver, but then again, that liver transplant  
2 would get reinfected with Hepatitis C again.

3 So it's not really an option as such in terms of  
4 long-term survival, it is more in terms of quality of  
5 life issues. A lot of the time my patients tell me,  
6 "I don't mind how long I live but I want to have a good  
7 quality of life. I want to live life. I don't want to  
8 be disabled. I don't want to have side effects. I want  
9 to do what I want to do." So therefore, even though you  
10 say to me that I could look at the response rates for  
11 the first 12 weeks, to decide how long the treatment  
12 will last for, they are not interested.

13 So it's very much of a personal choice. It is not  
14 the fact that clinicians do not want to treat, it's the  
15 fact that the patients have heard of the toxicity of the  
16 ribavirin/interferon treatment and the poor response  
17 rate, that deters them from taking Hepatitis C  
18 treatment.

19 Q. I think that's all I'm able to ask at the moment. There  
20 may be one or two other questions that we would like to  
21 ask and if those can be put into written form in due  
22 course, then I would appreciate being able to do that?

23 THE CHAIRMAN: I'm sure that that's perfectly appropriate as  
24 an approach. I think it might help if you ensured that  
25 there was some dialogue with Ms Dunlop and her team so

1           that if there are any consequential issues, they can all  
2           be dealt with at once and that way we would avoid going  
3           back to Professor Leen over and over again.

4   MR DI ROLLO:   Indeed.

5   THE CHAIRMAN:   So some sort of sensible common sense  
6           approach to it, I think, would be very helpful.

7   MR DI ROLLO:   Of course.

8   THE CHAIRMAN:   Professor Leen, can I come back to  
9           Mr Di Rollo's first question because the period he  
10          identified is, for a particular range of reasons, quite  
11          important to us, 1989 to 1990. The hypothesis he set  
12          out was one in which the patient didn't know that he was  
13          infected with HIV.

14   A.   But the clinician knew?

15   THE CHAIRMAN:   But the clinician knew. That's the second  
16          half of the hypothesis. And what might one have  
17          expected to happen in those circumstances about  
18          treatment? Do you have any feel for that at all?  
19          I know you weren't here, but you were in Manchester, of  
20          course, where the same problems might have arisen.

21   A.   I think that treatment is a two-way thing. It's not the  
22          doctor's decision, and one of the things which we were  
23          having to address is that this time was a sea change in  
24          terms of how doctors approached patients. One of the  
25          things that happened then -- it's all about empowering

1 the patient. You are faced with a life-threatening  
2 situation. You have the right to know that, you have  
3 the right to know what the doctors can or can't do for  
4 you at that time. For me it was completely different.  
5 My patients were telling me, "This is what I want. This  
6 is what I don't want to happen."

7 For me in my training I say, "Wow," because we  
8 always thought the doctors were the white coats, they  
9 knew what was best for the patients, and HIV was the  
10 thing which tells us, "Sorry, mate, the patient is king,  
11 we are here to serve the patient." That's what  
12 I learned. And I think that has changed medicine, not  
13 just in HIV, in most fields. So it is almost alien to  
14 me now to think about a physician withholding this  
15 information from the patient because it's crucial for  
16 the patient to know what is at stake.

17 So I can't fathom to think about how I would react  
18 to that. I don't know if it did happen, but if it did  
19 happen, I find it totally incredulous, about the whole  
20 thing.

21 So, therefore, the question is: would that clinician  
22 then offer to treat this patient with HIV with antiviral  
23 therapy, and if I was the patient, I would say, "Why am  
24 I taking this?" I don't know if the Internet would have  
25 been that wonderful in those days but I would have done

1           some research if I was a patient. But you are right, it  
2           depends on the patient as well, as to how much faith and  
3           how much they take from the doctor.

4           I can't prescribe something to a patient without  
5           explaining to them why I'm prescribing this and what the  
6           side effects are. So it would be very difficult for  
7           a clinician to convince a patient to take a drug unless,  
8           of course, the patient knows what it is for. So you  
9           need to tell them what they have got.

10   THE CHAIRMAN: It is fairly clear that among your  
11           patients -- and I'm sure it wouldn't be a generality but  
12           among your patients there were significant numbers of  
13           people who were very articulate and were well able to do  
14           their own research and confront you with in effect their  
15           demands for treatment.

16           I know I asked the other side of the question  
17           earlier on, but did that apply to all classes of  
18           patients that you saw or were there particular groups  
19           that were better informed?

20   A. I think the gay group was much better informed because  
21           it happened to them initially, and in a way the  
22           epidemic -- the reason why I went to London was because  
23           that's where it was happening in those days. Manchester  
24           was quite busy as well. Manchester, with a 5 million  
25           population in Greater Manchester, was quite busy with

1           them as well.

2           The gay group was much better informed, the drug  
3           users were not so much informed and I would have thought  
4           that the haemophiliacs -- I did not have many  
5           haemophiliac patients to look after in the early days  
6           but a lot of them are very intelligent anyway, so I'm  
7           sure they would have been able to do some research.  
8           When they were asked to take some medication, I'm sure  
9           they would have asked why, but I could be wrong.

10          But I would have thought that was what was happening  
11          in those days.

12   THE CHAIRMAN:  It's quite difficult to look back but I think  
13          that we know that the gay rights movement in Edinburgh  
14          did do a great deal.  We have seen the magazine, for  
15          example, and we know of their activity with the  
16          infectious diseases doctors here.  But you didn't have  
17          much to do with haemophilia patients at that time?

18   A.  No, I have got a few now because Dr Brettle has retired.  
19          I have inherited his patients.  But I can't comment on  
20          the haemophiliac group.

21   THE CHAIRMAN:  Mr Di Rollo, I'm anxious to tease out that  
22          period for reasons that will be obvious.  Is there  
23          anything else you want to ask at this stage about that  
24          or would you rather just reserve you position?

25   MR DI ROLLO:  I think we should just reserve the matter, if

1           that's fine.

2   THE CHAIRMAN: I think, Professor Leen, it looks highly  
3           likely that we will be asking you a few particular  
4           questions. You will appreciate that for all of us  
5           everything you say has an element of novelty to it and  
6           as one thinks over the issues later, particular problems  
7           arise. So if we may, we will come back.

8           Mr Anderson?

9   MR ANDERSON: I have no questions at present but clearly if  
10          matters arise because of further questioning --

11   THE CHAIRMAN: You would want to be involved.

12   MR ANDERSON: Clearly I may wish to be involved. But for  
13          the moment no, thank you.

14   MR SHELDON: No, thank you, sir.

15   THE CHAIRMAN: Thought processes are continuing over here,  
16          so shall we just wait a moment. (Pause)

17   A. May I say something as well on this issue about the HIV  
18          status?

19                We would not have done HIV tests on a patient  
20                without asking for permission to do HIV tests. That's  
21                crucial. So that's why it's all sort of alien to me.  
22                One of the things on my training was that you have to  
23                have an informed discussion with the patient about the  
24                pros and cons, what it means, life insurance issues, if  
25                we do the test.

1           So, to me, doing a test without consulting the  
2           patient is the first question that one has to ask: why  
3           was that done in the first place? Was it part of  
4           a research thing? Was it because of patient care?

5           Does that answer your question?

6   THE CHAIRMAN: Up to a point, except that, while I would  
7           have no difficulty accepting that as a generality now, I  
8           am not confident yet that I have got a clear enough  
9           picture over the whole span of time with which this  
10          Inquiry is concerned.

11          So I would have to ask back, in response to that  
12          comment, when you had that training and when did that  
13          particular protocol embed itself in your consciousness.

14   A. I was just thinking about that when I was talking to  
15          you. When I was starting in 1986 in clinical  
16          medicine -- because I was in research before that --  
17          that was the first thing I was taught. In 1986 we had  
18          to do that. The timeframe you are talking about?

19   MR DI ROLLO: We are dealing with the period, I think, from  
20          about 1984 onwards, 1983/1984.

21   A. That's two years before I started my training. I need  
22          to do some research to find out, if I could. I don't  
23          think there was any guidelines. I think there were some  
24          almost unspoken rules about how to do tests. But I'll  
25          try and look it up for you and see what there is in

1 terms of guidance for doing those tests.

2 THE CHAIRMAN: That would be helpful, if you have a look at  
3 it.

4 Now, Ms Patrick, has the process resulted in  
5 a question?

6 Further questions by MS PATRICK

7 MS PATRICK: I have one more question, sir, please,  
8 referring to the hypothetical situation that we have  
9 been discussing, which is that the patient doesn't know  
10 the positive result of his HIV test but the clinician  
11 does know. What would you think if the patient did not  
12 have any symptoms and didn't need treatment? In the  
13 second half of the 1980s.

14 A. That's a very good question. I think we are now facing  
15 somebody whereby no intervention would probably be  
16 offered anyway and then one probably views this doctor  
17 as being totally paternalistic and taking all the risks  
18 and making all the decisions.

19 So I think again it would go back to why was the  
20 test done in the first place and whether or not the  
21 doctor feels guilty of opening up a can of worms and not  
22 knowing how to cope with that. So, therefore, it is  
23 possible that the doctor is waiting for the right time  
24 to break the news, bearing in mind that it is a life  
25 sentence at the time. You have got this horrible



1 condition and you have got nothing to offer them. So  
2 I can see that point of view as well.

3 But that's the whole thing about looking for things  
4 that you shouldn't be looking for. What do you do with  
5 the results? That is crucial and, yes, it may well have  
6 happened because, I guess, in terms of looking at  
7 haemophiliacs and the rest of it, (inaudible) that we  
8 are looking if there's a problem in the area, they would  
9 have done that.

10 But in hindsight one other advice is that you  
11 anonymise all the names so that you just know there is  
12 a problem and then, once you know there is a problem,  
13 then you then approach the patients. But that's  
14 hindsight; you have got lots of decades of knowledge and  
15 wisdom.

16 So in those days, yes, you are right, it's difficult  
17 to say, yes. Does that answer your question?

18 Q. It does. Thank you very much.

19 THE CHAIRMAN: Professor, thank you very much indeed.

20 I think you, from your point of view, have been living  
21 through a very challenging and interesting era.

22 A. It has been amazing, very fulfilling, because, as I say,  
23 it is not just drugs, it's caring, it's the human side.  
24 It's different now, obviously, because the disease is so  
25 manageable. But it was amazing.

1 THE CHAIRMAN: Thank you very much. We will adjourn.  
2 (1.00 pm)  
3 (The short adjournment)  
4 (2.00 pm)  
5 PROFESSOR CHARLES FORBES (continued)  
6 Questions by MR GARDINER  
7 THE CHAIRMAN: Good afternoon, Professor Forbes.  
8 A. Good afternoon.  
9 THE CHAIRMAN: Mr Gardiner?  
10 MR GARDINER: Yes. Thank you, sir.  
11 Professor Forbes, good afternoon.  
12 A. Good afternoon.  
13 Q. You have previously appeared before the Inquiry in  
14 connection with the B2 topic and that was on 28 April  
15 and of course, today, I'm primarily asking you questions  
16 about the B5 topic. The Inquiry asked you for  
17 a statement about topic B5 and sent you a schedule which  
18 listed the matters which we were asking you to include  
19 in your statement and that is [\[PEN0120362\]](#).  
20 Do you have that?  
21 A. Yes, thank you.  
22 Q. Thank you. So these are the questions which we were  
23 asking you to address and you kindly produced  
24 a statement, which is listed in our database at  
25 [\[PEN0120411\]](#). Do you have a copy of that?

1 A. Yes, thank you.

2 Q. Okay. So we are going to have to work between these two  
3 documents as best we can.

4 Just to get some context here, Professor Forbes,  
5 could you tell us in 1983/1984 how many haemophilia  
6 patients you had under your care?

7 A. Approximately 250 with Haemophilia A and B. But in  
8 addition there were other more unusual conditions like  
9 von Willebrand's disease. So the numbers went up to 300  
10 or 400.

11 Q. Thank you. Which other doctors did you have to help you  
12 to treat those patients in 1983 and 1984?

13 A. We had a small team of doctors, mostly people who were  
14 there in training and they included a Dr Gordon Lowe,  
15 who is now professor and now retired, and a cohort of  
16 more junior people, who are not named here.

17 Q. Yes. When you say that Professor Lowe, as he now is,  
18 was "in training", could you explain a little bit more  
19 what you mean by that?

20 A. Well, he came to the unit as a senior registrar, which  
21 was -- it's a grade that has now actually disappeared  
22 but it was the senior of the staff in training, towards  
23 the end of their training. So he would come for three  
24 or four years to be rounded off, as it were.

25 Q. I presume that at that stage a senior registrar would be

1           able see patients on his own and prescribe treatment and  
2           so on?

3    A.   Oh, certainly.

4    Q.   I'm just a little bit curious about your use of the  
5           phrase "in training"?

6    A.   That's the phrase that is used because they have  
7           a training period that goes up to the time at which they  
8           are appointed a consultant, wherever.

9    Q.   So is it training in haematology?

10   A.   It was training in general medicine, with a special  
11          interest in haemophilia.

12   Q.   Thank you.  If we could go to the questions document and  
13          look at the first two questions which we have asked you  
14          to consider.  The questions are:

15                 "When factor concentrates became available in the  
16                 early 1970s, did Professor Forbes discuss the risks of  
17                 using factor concentrates (for example, infection with  
18                 Hepatitis B and, subsequently, NANB hepatitis) with his  
19                 patients?"

20                 The next question is:

21                 "Did Professor Forbes discuss the relative risks of  
22                 using cryoprecipitate as opposed to factor concentrates  
23                 with his patients?"

24                 Your answer in your statement, which is 0411, is:

25                 "I started to work with haemophiliacs in 1965 in the

1 Royal Infirmary in Glasgow, having spent the previous  
2 year in East Africa working with Professor AS Douglas,  
3 who was the haemophilia director in Glasgow at that  
4 time. I have been asked to make comments from 1981  
5 until 1987, which was a time of great change in  
6 haemophilia care with the development and knowledge of  
7 both HIV infection and the consequences of Hepatitis C  
8 as it became known."

9 Then the next paragraph:

10 "At that time the usual policy for haemophilic  
11 bleeding was the use of pooled cryoprecipitate."

12 When you say "at that time", what time are you  
13 talking about in that paragraph, Professor Forbes?

14 A. This is the 1970s to early 1980s.

15 Q. Thank you:

16 "The amount given depended on the severity of the  
17 disease in the individual patient and also the type of  
18 procedure that was required for the amount of trauma  
19 that had been given to the patient."

20 Then paragraph 3:

21 "I think at this time ..."

22 And you are still talking about that period, are  
23 you?

24 A. Yes, yes.

25 Q. "... we were all aware of the potential problems of all

1 material of blood origin being given to individuals and  
2 we did monitor them for changes in liver function tests  
3 which at that time was probably the best and only  
4 available test. In particular, changes in liver enzymes  
5 were a good indicator of infection. We quite rapidly  
6 became aware that there were probably different types of  
7 hepatitis, short incubation hepatitis and a longer  
8 incubation hepatitis, and certainly some in between. We  
9 were also aware that the chances of developing hepatitis  
10 were lower with locally harvested cryoprecipitates as  
11 opposed to concentrates which were made with  
12 indeterminate but huge numbers of patients' plasma being  
13 pooled together. So generally we tended to favour the  
14 use of cryoprecipitate and that continued for many  
15 years."

16 I'm not sure if you have addressed the question of  
17 whether you discussed the risks that there were for your  
18 patients in using these products. Can you remember if  
19 you would have discussed them in this time period?

20 A. I think it would be very reasonable to have discussed  
21 them and that would have been our policy at that time.  
22 In particular, we would be interested in following them  
23 after they have had blood products of any type,  
24 especially concentrate, and we would be interested to  
25 follow their liver function to see if it was affected

1 and get some handle as to any complications that may  
2 have arisen. So they would certainly have been told  
3 that there was -- and it was well-known -- that there  
4 was a possibility of hepatitis resulting from the use of  
5 concentrates or cryoprecipitate.

6 Q. Yes. Would you have explained the difference between  
7 short incubation and longer incubation hepatitis to your  
8 patients?

9 A. No, I don't think that would have been particularly  
10 relevant. We would certainly want to follow them over  
11 a period of time. I don't think we understood very much  
12 about the different types of hepatitis but there  
13 certainly was a short incubation and a long incubation  
14 type and an intermediate one as well.

15 Q. Yes.

16 A. And that over subsequent years has become very apparent  
17 and they all are due to different viruses.

18 Q. Just focusing on what you would have discussed with your  
19 patients, would you have discussed the relative risks of  
20 using cryoprecipitate as opposed to concentrates in  
21 terms of contracting hepatitis?

22 A. There is no doubt that the use of concentrates was  
23 associated with a greater incidence of hepatitis. Just  
24 because of the number of donor exposures that resulted.  
25 For example, the concentrates, some of them might

1 include blood from 20 or 30,000 donors. So that  
2 multiplied the risk greatly.

3 Q. Yes, and would you have explained that to your patients?

4 A. I think we tended not to use the concentrates for that  
5 reason and that was certainly explained to the patients.

6 Q. Yes, thank you. If we go on to question 3:

7 "Did Professor Forbes discuss the possibility of  
8 DDAVP with mild haemophiliacs? Did he treat mild  
9 haemophiliacs with DDAVP?"

10 In your answer you say:

11 "We were also very aware of the possibility of using  
12 DDAVP in patients with mild disease who were having  
13 small traumas or small surgery. This we widely accepted  
14 and was really very successful for a day or two's  
15 treatment only, for example one or two teeth or a very  
16 small procedure. During this time we also became aware  
17 of the other long-term implications of DDAVP,  
18 particularly with fluid and electrolyte retention. So  
19 it was used with some caution."

20 The next question is:

21 "When the possibility that AIDS was a blood-borne  
22 disease which affected haemophiliacs became apparent  
23 (around December 1982), did Professor Forbes discuss the  
24 implications with his patients before continuing to use  
25 factor concentrate therapy?"



1           Your answer is paragraph 5 where you say:

2           "I think very early on in the progress of the virus  
3 story, we became aware that AIDS was a blood-borne  
4 disease probably transmitted by Factor VIII perhaps more  
5 often by concentrates than cryoprecipitate."

6           Just pausing there, Professor Forbes, when you say  
7 "very early on", what time period are you talking about?

8 A. Well, I think we are talking of months rather than  
9 years, and it became apparent that the concentrate made  
10 from such large numbers of donor volumes of plasma were  
11 so enormous that it was inevitable that there was going  
12 to be transmission of disease.

13 Q. Focusing specifically on --

14 A. Concentrate. Cryoprecipitate. The pool of donors from  
15 local sources -- that's Scottish cryoprecipitate -- was  
16 much less likely to transmit a virus.

17 Q. Yes. I mean, I'm really looking for a date here from  
18 you, Professor Forbes, in this paragraph, where you say:

19           "I think very early on in the progress of the virus  
20 story ..."

21           When you became aware.

22 A. It's quite difficult thinking back to an actual date but  
23 it was early on. We were very rapidly aware that  
24 something nasty was happening with transfusion and the  
25 cases coming from America were quite clearly going to be

1 mirrored in the UK, and we were cautious about using  
2 concentrate for that reason.

3 Q. Yes.

4 A. Whether that was wise or not, I think it probably was.

5 Q. Yes. I wonder if it would help to look at what you told  
6 us when you were last here, talking about the B2 topic.  
7 So if we could have a look at the transcript for that  
8 day at page 102, now. If you see around about line 6,  
9 and the context here is the chronology of the developing  
10 story of the virus, as you put it, we see:

11 "On 22 March 1983 there was a meeting of the  
12 haemophilia and blood transfusion working group at  
13 St Andrew's House."

14 And you were there. If we just go down that page,  
15 Professor Forbes, we see that there are a number of  
16 issues discussed at that meeting. One of them was the  
17 development of heat-treated Factor VIII. Then if you go  
18 over the page to page 103, at the top of the page, line  
19 1:

20 "I think the clinical trials were the only way ahead  
21 at this time. So we were happy to do that."

22 Then the question is:

23 "And then AIDS was discussed."

24 Do you remember discussing this the last time you  
25 were here, Professor Forbes?

1 A. Yes.

2 Q. So we see that this is a meeting in March 1983 and AIDS  
3 is being discussed. If we go half way down the page at  
4 line 14, the question is:

5 "Do you have any memory of this meeting,  
6 Professor Forbes?

7 "Answer: I have to say, I don't remember the  
8 meeting but the sentiments were quite clear and there  
9 was a wave of tremendous anxiety about HIV infection and  
10 its transmission."

11 I think the next bit is important:

12 "And a lot of depression in the group of patients  
13 who were being exposed to the chance of infection."

14 Then reading on:

15 "Question: That particular recorded concern, as  
16 at March 1983, was a concern that AIDS might appear in  
17 the UK; do you think that was the extent of the concern?

18 "Answer: I think most people thought it undoubtedly  
19 would appear in the course of time and already we were  
20 starting to look rather differently at our patients to  
21 see if they had any of the features that might be an  
22 early warning of AIDS."

23 Then if you could turn now to page 110, there is  
24 a continuing discussion about this risk in the pages in  
25 between, Professor Forbes, but if you look at the bottom

1 of the page there is a question to you:

2 "Well, are you saying that that altered your  
3 practice in Glasgow in 1983?"

4 This is the emerging story, and over the page you  
5 say:

6 "Well, it was a concern.

7 "Question: And recognition of that as a concern,  
8 what effect did that have?

9 "Answer: Well, we were scratching our heads and  
10 asking: what is best to give patients? Many took the  
11 view that the major problem was not something that would  
12 happen in the future, like HIV disease or AIDS, but the  
13 concern was would the patient bleed and die at that  
14 point. So the tendency was to come down on the side of  
15 using whatever concentrate we had available or  
16 cryoprecipitate. So treatment was still the option of  
17 choice."

18 I'm showing these bits, Professor Forbes, to see if  
19 we can tease out the date from paragraph 5 in your  
20 answer. It certainly seems that by March 1983  
21 clinicians are aware of the risk. Would you agree with  
22 that?

23 A. I think it was coming up on the horizon. I think we  
24 knew so little about it, even from the American  
25 experience, that we were not clear just what was going

1 on. But we understood enough about it to be concerned  
2 at that time.

3 Q. Yes.

4 A. But what do you do about it? You have to find out the  
5 cause, which took a long time, and also what to do about  
6 it, which took a long time. And there were false  
7 avenues all the time in our attempts to get round the  
8 problem.

9 Q. The context of my questions are very much information  
10 given from doctor to patient. So just to recap about  
11 what we have looked at: in the transcript you said that  
12 by about March 1983 you had been looking at your  
13 patients differently to see if there was any early  
14 warning of AIDS?

15 You say that at that time your preference was to  
16 come down on the side of continuing to use concentrates  
17 and cryoprecipitate, and you say that there was  
18 depression in the group of patients who may have been  
19 exposed.

20 I wonder, does that help you answer my question,  
21 Professor Forbes: what were you telling your patients at  
22 this stage about the risk of getting this disease by  
23 using these products?

24 A. The bottom line of that is that no matter what you had  
25 to treat them, if you didn't treat them they might

1           certainly die of bleeding, and that, up until the 1970s  
2           and 1980s, was the usual problem. So that didn't  
3           change. And we had to say to them, "Look, you have to  
4           have treatment," there is no way that we can't just say,  
5           "Well, we will not give you anything and that will  
6           protect you against this supposed danger that is now  
7           looming up". And we all did accept that something was  
8           happening. We weren't sure. At that time it was mainly  
9           the anxiety about AIDS rather than hepatitis, which  
10          didn't seem to be such a great problem, although we knew  
11          it was happening.

12                 So the bottom line was that they still had to be  
13          treated and you had to choose what you considered the  
14          safest product from all points of view.

15         Q. Did you advise your patients that this was the option  
16          that you recommended, continuing with treatment?

17         A. Yes, it was the right option as well for them, if they  
18          had a bleeding problem.

19         Q. Yes. That's what you advised them? You told them of  
20          the risk and you advised them to continue with the  
21          treatment. Is that your evidence?

22         A. Yes.

23         Q. Thank you.

24         A. They were very aware of the problems which were widely  
25          talked about in the media, with some hysteria, I have to

1 say. And there was a lot of anxiety and the sensible  
2 ones in fact agreed that they had to have their  
3 treatment and they got usually cryoprecipitate but not  
4 always.

5 Q. Yes. Could we just go back to paragraph 5, just to  
6 finish that off? Just reading from the third line:

7 "This advice was given to individual patients but as  
8 most the patients were getting cryoprecipitate, the  
9 question of concentrate therapy arose only infrequently  
10 and patients were told about the implications,  
11 particularly with regard to HIV infection. The end  
12 result of course was that we tended to favour the use of  
13 cryoprecipitate and that is what our policy was."

14 So just pausing there, you would encourage your  
15 patients to opt for cryoprecipitate as opposed to  
16 concentrates?

17 A. It depended on the problem that we were faced with. If  
18 it was a minor/moderate bleed, then cryoprecipitate  
19 seemed to us to be much safer, and it was only if it was  
20 a major bleeding problem or major surgery that was  
21 needed, would we use concentrate. And that was our  
22 advice at the time.

23 Q. Yes. Is that what you advised your patients,  
24 Professor Forbes?

25 A. Yes.

1 Q. Did you wait for the patient to raise that issue or is  
2 that something that you would raise yourself?

3 A. Well, we would always discuss what we were going to do  
4 because most of these were -- there was an element of  
5 choice for the patient and I think that we would always  
6 give them what we considered the best advice, which was  
7 the use of cryoprecipitate.

8 Q. Yes. Thank you. If we could move on to question 6,  
9 please, the question is:

10 "When Professor Forbes became aware that  
11 pharmaceutical companies such as Alpha Therapeutics and  
12 Miles/Cutter had been granted a licence to sell  
13 heat-treated Factor VIII in the USA in February 1984 and  
14 that the products were available to clinicians in the UK  
15 on a named-patient basis, did he consider switching his  
16 patients to it? Did he discuss ..."

17 And I think that should be:

18 "... the relative safety of heat-treated, as opposed  
19 to non-heat-treated products."

20 Your answer at paragraph 6 is:

21 "Against this background we became aware that the  
22 HTLV-III virus was transmitting the disease in our  
23 patients. It was with some excitement that we heard  
24 that heat treatment of the plasma was a possibility and  
25 the date of this was 1984. There was, however, a lot of



1 concern about how effective this was and indeed one of  
2 the early heat-treated concentrates clearly had  
3 transmitted the virus and that set us all back and it  
4 took some time to return to a degree of confidence in  
5 the heat treatment process."

6 Professor Forbes, do you recall if you ever  
7 discussed the possibility of using American heat-treated  
8 products with your patients?

9 A. I think we thought there wasn't enough evidence to say  
10 that they were totally safe at that time. We were a bit  
11 anxious that the heat treatment which was being proposed  
12 would in fact destroy the Factor VIII activity and it  
13 would make it not useful to use, and that was certainly  
14 a view that I personally held. And it was only when the  
15 clear evidence with studies came from the USA that we  
16 started to believe that this was a possibility.

17 I would just remind you that there was this terrible  
18 episode where heat-treated material did transmit HIV  
19 infection to a cohort of patients and that really did  
20 set us back. We thought, "Gosh, this has not worked at  
21 all, and here we have a new cohort of people treated  
22 with heated material which has clearly not been  
23 effective". And that required more studies and further  
24 studies with a longer heating and a higher temperature  
25 to get rid of the HIV virus, the HTLV-III.

1 Q. Is it possible that that was in 1986, Professor Forbes,  
2 that that happened?

3 A. It could well have been. These things all took time and  
4 obviously, once someone has had the idea of heat  
5 treatment to get a safe product, it does take time and  
6 study and it could well be 1986.

7 Q. Yes. Thank you. I would like to ask you a few questions  
8 about immunological testing in Glasgow and you have  
9 kindly provided us with a separate statement about that,  
10 which is [\[PEN0121328\]](#).

11 A. Yes, thank you. I have it.

12 Q. Thank you. The Inquiry's questions are at [\[PEN0120771\]](#).  
13 There should be a schedule attached to that, if we go to  
14 the next page, please.

15 A. Thank you.

16 Q. Yes.

17 A. I have it.

18 Q. Thank you. The schedule sets out the questions that we  
19 would like you to address. Question 1 talks about the  
20 enclosed BMJ article, published on 15 October 1983, and  
21 entitled "Immunological abnormalities in haemophilia:  
22 are they caused by American Factor VIII concentrate?"  
23 And this reported a study of cellular immunity in  
24 a group of 19 haemophilia patients.

25 We have posed certain questions about that study. I

1 think we did touch on this when you were last here, this  
2 study, and if we could just have a look at the actual  
3 article, which is at [\[LIT0010215\]](#).

4 A. Yes, thank you, I have it.

5 Q. That's the article that we are talking about, isn't it?

6 A. Yes.

7 Q. Professor Forbes. Just looking at your answer,  
8 paragraph 1.1, you say:

9 "This bit of evidence starts in the early part of  
10 1983 when it was apparent that a variety of  
11 investigators had been finding some evidence of  
12 immunological abnormalities in patients with haemophilia  
13 ..."

14 And you cite several papers there. The next  
15 paragraph:

16 "All of these papers suggested that immunological  
17 abnormalities were occurring in patients who had  
18 received multiple infusions of Factor VIII and IX  
19 concentrate. We therefore undertook to look at our own  
20 patients to see if any abnormalities were occurring in  
21 them as a result of concentrate infusion. This indeed  
22 we did find and we thought there might be an association  
23 with the use of Factor VIII concentrates. The  
24 co-authors ... Drs Frobel, Madhok et cetera."

25 And:

1            "They all worked within the haemophilia centre at  
2            Glasgow Royal Infirmary and in the related section of  
3            immunology of that department."

4            In 1.3 you talk about the paper and explain that it  
5            consisted of some tests carried out on patients with  
6            haemophilia who had had multiple infusions. And at 1.4  
7            you explain that:

8            "When a variety of our unselected patients were  
9            compared against controls, there was a very significant  
10            diminution in the numbers of T4 helper cells and this  
11            reached conventional levels of significance. It is to  
12            be admitted the groups were not large enough to be just  
13            haemophiliacs treated with one or other of the various  
14            blood products which were available ..."

15            And so on. We are interested in information to  
16            patients in this section of the Inquiry,  
17            Professor Forbes, and you address that at paragraph 1.5,  
18            where you say:

19            "These 19 patients were all treated at the  
20            haemophilia centre at Glasgow Royal Infirmary but all  
21            had had different treatments over the preceding years.  
22            The purpose of the study, of course, was to find out if  
23            there was any evidence that patients who had had  
24            multiple transfusions with various products had any  
25            evidence of alteration of their immunological status and

1 I think that quite clearly ... did."

2 You say:

3 "The patients were aware that studies were being  
4 carried out as blood was asked for but they were not  
5 informed in great detail of the implications of the  
6 study. I don't think they were ever told that there  
7 were implications because I'm not sure that we knew if  
8 there were implications or not."

9 So could you expand a little bit on that paragraph,  
10 Professor Forbes. You say the patients were aware that  
11 studies were being carried out as blood was asked for  
12 but not informed in great detail of the implications of  
13 the study. What do you mean exactly by that?

14 A. I don't think we at that time could have predicted what  
15 the implications were or what the results would be.  
16 When the tests had been done, it clearly shows in fact,  
17 in this paper that we are talking about in the British  
18 Medical Journal, that there was a very significant  
19 difference in the tests that we were using. And,  
20 remember, these at that time were pretty crude and  
21 primitive tests. But clearly, in a well conducted study  
22 of normals and the patients, which is in table 1, there  
23 is a significant difference. So using a very simple  
24 test, we were able to show that there was suppression of  
25 the immunological function in these patients.

1           Whether that was due to the transfusion of products  
2           over a prolonged period of time, we were able to show  
3           that that was possibly true but. Whether it was  
4           absolutely true or not was in some doubt. Could it be  
5           that there was anything else happening at the same time  
6           that we weren't aware of? And we were very cautious in  
7           drawing our conclusions. These patients all were  
8           informed what was happening because they volunteered to  
9           give blood and all these tests were carried out on fresh  
10          blood samples taken from them.

11        Q. When you say they volunteered to give blood, how did  
12          that come about?

13        A. Well, they were just asked if they would mind giving  
14          a sample of blood, that we were going to look at some  
15          immunological tests that required fresh blood samples,  
16          to look at their cells and see if there was anything  
17          happening that we should know about.

18        Q. Yes.

19        A. So it wasn't written informed consent because that  
20          really didn't exist at that time.

21        Q. So who would have asked them about that,  
22          Professor Forbes? Did you do that?

23        A. Probably mostly me but we had other people working with  
24          us. Dr Madhok, who was a rheumatologist and very  
25          interested in immunology would have asked. He also

1 looked after some of the patients, being joint disease.  
2 He was interested in the haemophilic joint disease. So  
3 he was a well-known physician to them. Gordon Lowe, is  
4 also on the paper, but it was done by the staff of the  
5 unit.

6 Q. You say that after the study was completed, the  
7 implications weren't communicated to the patients and  
8 you say that you are not sure if you knew if there were  
9 implications or not. But what do you mean by that?

10 A. I don't think we understood what was really happening.  
11 We were able to show that using these particular tests,  
12 no matter how primitive they were, there was something  
13 happening and it seemed to be associated with the amount  
14 of material given to them.

15 Whether it was a direct effect of some component of  
16 the blood products given, we weren't clear. So this was  
17 very much a preliminary paper, suggesting that there  
18 were immunological abnormalities. What they meant,  
19 I don't think at that time we knew, and I'm not sure  
20 that we even know at this time.

21 Q. Yes. Is that why you didn't go back to the patients and  
22 explain the results of the study?

23 A. We didn't know what they meant.

24 Q. Thank you. If we could just put that aside for one  
25 moment and go back to your main statement, please. So

1 we can continue chronologically. I think we are now at  
2 question 7, so if you could look at question 7.

3 A. Yes.

4 Q. The question -- if you have that, Professor Forbes?

5 A. Yes, I have it.

6 Q. "When did Professor Forbes start testing his patients  
7 for HTLV-III?"

8 I'll just read the next question as well:

9 "In when circumstances were these blood tests  
10 carried out? When were blood samples taken from his  
11 patients? Were the blood samples taken with the  
12 intention of testing for HTLV-III? Who carried out the  
13 tests?"

14 Your answer to that is at paragraph 7 and you say:

15 "Despite the fact that we guessed that the virus was  
16 transmitted in blood products, we did not have any test  
17 for the virus itself and it was therefore decided that  
18 we should collect samples from patients with a view to  
19 storing them until a test became available."

20 Professor Forbes, who decided that samples should be  
21 collected?

22 A. Well, I think it was very important from the  
23 epidemiology of -- and for us to enhance our knowledge  
24 of what was happening, that we did have samples that we  
25 could, because we believed that there would be a test



1 for this virus if such a virus existed, and that we  
2 should in fact be prepared for this day in the future,  
3 when an accredited test was available, and that was why  
4 I decided that we had to collect samples. And in fact,  
5 we had been doing that for some time with a view to  
6 looking at other things that might happen in the blood,  
7 particularly from the point of view of immunological  
8 changes. But we then started to think about a virus as  
9 it became clear that it probably was a virus. But not  
10 any stronger than that.

11 Q. So approximately what time did you start collecting  
12 samples?

13 A. Well, that's difficult to put a date on it but we had  
14 been collecting for some months certainly, to build up  
15 a battery of samples collected, even from the same  
16 patients, over the period of time, to see if things were  
17 going to change in the future.

18 Q. Yes. When would you have started? You say for some  
19 months?

20 A. Well, I think that the best I can say is that it  
21 certainly was months. I don't think it was years but we  
22 then had a collection that could be tested in the  
23 future.

24 Q. Yes. So is it May 1983 that you started collecting  
25 samples?

1 A. It may even have been before that. I just don't  
2 remember the dates at this time.

3 Q. Thank you. So just reading on there, paragraph 7:

4 "This happened very slowly over several years and it  
5 was through our association with Dr Mads Melbye that we  
6 got access to early testing on special samples. It was  
7 by doing this that we were able to show that many of the  
8 patients were already positive at the time the test came  
9 on stream."

10 Just pausing there, do you recall, Professor Forbes,  
11 whether the patients were told that their blood was  
12 being stored for later testing?

13 A. I don't think we did tell them at the time but the  
14 memory is very hazy as to what was said. We certainly  
15 told them that we were taking blood to test probably in  
16 the future. The implication would be that these were  
17 stored samples.

18 Q. Yes. Thank you. Just reading on to the next paragraph,  
19 you say:

20 "The initial samples were taken over a period of  
21 several years. As I say, these tests were carried out  
22 as a special favour by Dr Mads Melbye, I think in his  
23 laboratory in Denmark. Thereafter, our local  
24 virologist, (Dr Eddie Follett) at Ruchill Hospital, had  
25 set up a laboratory in which he could do the test and

1           thereafter they were routinely done there by him and his  
2           colleagues."

3           We have been trying to work out the dates by looking  
4           at the literature. Could we have up, please, page 4 of  
5           [\[DHF0026016\]](#)? You should have a hard copy of that. The  
6           first page says "The Lancet" and it's at page 5 of the  
7           document.

8           A. Thank you, I have it.

9           Q. We see the heading of this article is:

10                   "HTLV-III seropositivity in European haemophiliacs  
11                   exposed to Factor VIII concentrate imported from the  
12                   USA."

13                   This is the study which you carried out with  
14                   Dr Melbye. Is that right?

15           A. Yes. He was the person who is the virologist first of  
16           all, working out of Denmark, but he approached us to see  
17           if we had any samples from patients with haemophilia who  
18           had been treated over a prolonged period of time, which,  
19           of course, we did have.

20           Q. Yes. If we just look at the authors of the report, we  
21           have Dr Melbye, Dr Madhok and then we see also  
22           Professor Lowe. Is that right?

23           A. Yes, yes.

24           Q. And Karin Froebel?

25           A. She was a local immunologist in Glasgow.

1 Q. Thank you. Then your own name and then we see  
2 Robert Gallo. Are we right in thinking that Dr Gallo  
3 would have provided Dr Melbye with the isolate for the  
4 virus, to allow the testing to be done?

5 A. I think that was how it had worked. He was the American  
6 who was credited as being one of the co-discoverers of  
7 the HIV virus.

8 Q. So that's how the test could be done?

9 A. That's how the test was done and I'm sure that he  
10 provided the isolate that enabled Dr Melbye to actually  
11 do them, to set them up.

12 Q. Yes. If we look at the summary, we see:

13 "77 Scottish haemophiliacs and 22 Danish  
14 haemophiliacs were serologically tested for antibodies  
15 to HTLV-III virus. Since 1979 the Scottish patients had  
16 been treat largely with Factor VIII concentrate produced  
17 in Scotland, whereas all but two of the Danish patients  
18 had received both locally prepared concentrate and  
19 commercial concentrate made from US donor material.  
20 15.6 per cent of Scottish and 59.1 per cent of Danish  
21 haemophiliacs were antibody positive."

22 So 15.6 per cent. That's 12 patients -- is that  
23 right -- that were positive?

24 A. Absolutely.

25 Q. If we look over the page to 6020 in the left-hand

1 column, we see just at the top left:

2 "Similar data were obtained on Scottish  
3 haemophiliacs enrolled in the Regional Haemophilia  
4 Reference Centre, Glasgow. Blood was taken from these  
5 patients between December 1983 and July 1984."

6 Dr Forbes, do you think that those are the blood  
7 samples that you have just been telling us about, the  
8 ones that were stored for later testing?

9 A. Yes.

10 Q. Thank you.

11 THE CHAIRMAN: Dr Forbes, are these then different patients  
12 from those who were dealt with in the 1983 letter?

13 A. No, I think that they probably include representatives  
14 from the 19.

15 THE CHAIRMAN: Well, it worries me just a little that  
16 I can't square the information. If you look at the  
17 right-hand column on page 1445 of the hard copy, there  
18 is information that 40 per cent of the subjects had  
19 received commercial factor concentrate either alone or  
20 in combination, whereas, as you previously told us, the  
21 patients who were in the 19 included only two, I think,  
22 who had received --

23 MR GARDINER: I think that might include the Danish ones as  
24 well, sir.

25 THE CHAIRMAN: No, it's "in Scotland".

1 MR GARDINER: Okay.

2 THE CHAIRMAN: As shown in table 1. Do you think that's  
3 everybody, Danish as well as ...? I don't think so.  
4 There are two separate groups of paragraphs.

5 A. Yes, I understand that.

6 THE CHAIRMAN: I think, the Danish come, 22, and then  
7 comments about that and then "In Scotland ..." We have  
8 the following details.  
9 So at the moment I'm not getting the arithmetic to  
10 work. I think it's as simple as that. If they are  
11 overlapping groups, then they seem to overlap in  
12 a rather strange way, and of course that raises the  
13 question about whether samples were being collected from  
14 the two different groups. I would like, if possible, to  
15 be able to get some reconciliation or some explanation.

16 A. Well, I suspect it may not be all the 19 that were  
17 tested originally. That's the only thing I can suggest  
18 at this time. I don't know if that helps at all.

19 THE CHAIRMAN: It may be that we just have groups that may  
20 overlap. I think we may be back to Ms Dunlop's Venn  
21 diagrams with a small overlapping section in the middle  
22 somewhere. Clearly neither group represents the whole  
23 constituency that you had available.

24 A. Absolutely not.

25 THE CHAIRMAN: Yes.

1 A. Can't.

2 MR GARDINER: Sir, we are trying to find the section where  
3 it mentions the 40 per cent.

4 THE CHAIRMAN: 40 per cent is in the first page.  
5 40 per cent is the -- I'm losing my hard copy  
6 references -- is on page 1445 of the Lancet article  
7 of 22 December, 1984. It's immediately above the  
8 discussion.

9 MR GARDINER: I think it's 40 per cent of the patients that  
10 had received commercial concentrates, as opposed to 40  
11 of all of them.

12 THE CHAIRMAN: So it's the bottom section of the table, is  
13 it, that's referred to in that paragraph? Which doesn't  
14 work for me since it's two people representing  
15 40 per cent of 25: I'm not sure that's right.

16 MR GARDINER: It's the patients that have received  
17 commercial concentrate, whether Scottish or Danish and  
18 it's 40 per cent of that group, sir; I think.

19 THE CHAIRMAN: Two out of 25? Two out of 25, if that's what  
20 the 40 per cent refers to. So there is a problem.

21 PROFESSOR JAMES: I have this now. So in this section  
22 called "healthy haemophiliacs" there is first  
23 a paragraph referring to the 22 Danish haemophiliacs.  
24 There is, second, a paragraph starting:  
25 "In Scotland ..."

1           There is then a paragraph referring to table 1,  
2           which actually combines Denmark and Scotland. So that  
3           the 40 per cent is of the individuals from both Denmark  
4           and Scotland who received either commercial or both, and  
5           that comes out at 39.6 or 40 per cent. That's where the  
6           40 per cent comes from.

7   THE CHAIRMAN: I think I can see it is rounded up to  
8           40 per cent. I just still can't get --

9   PROFESSOR JAMES: The important thing is that the sentence:  
10           "40 per cent of subjects receiving commercial factor  
11           concentrate either alone or in combination with local  
12           products ..."

13           Refers to both Denmark and Scotland put together.

14   THE CHAIRMAN: Did this article make a great impact at the  
15           time, Professor Forbes?

16   A. I don't think we ever know what impact our work makes.

17   THE CHAIRMAN: Maybe people are still trying to work out  
18           what it refers to.

19           Anyway, I don't think that I have resolved the basic  
20           question, whether the populations are the same or  
21           different or how they were selected or when.

22   MR GARDINER: We can continue considering that, perhaps, and  
23           I'm sure we will resolve it.

24           Professor Forbes, could we just pass on to the next  
25           question now? The question is:



1           "Did Professor Forbes tell his patients that  
2           HTLV-III tests were being carried out? Did he obtain  
3           consent from his patients before carrying out the  
4           HTLV-III tests?"

5           Then question 10:

6           "Did Professor Forbes' practice in relation to  
7           obtaining consent and testing patients for HTLV-III  
8           change between 1984 and 1987?"

9           You have answered that at paragraph 9 of your  
10          statement and what you say is:

11          "The next question that you ask about is did the  
12          patients get told they were being tested, and I think  
13          the answer is a changing one. From the early days in  
14          1980 or so until the tests became routinely acceptable,  
15          they were probably not told much about it. I don't  
16          think that we actually asked for consent for the samples  
17          to be specifically tested, but as in all these areas  
18          things tighten up and then consent was asked for and  
19          eventually (informed consent) written."

20          Just pausing there, just thinking about the samples  
21          that were tested in the study that we have just looked  
22          at, you have told us that at the time samples were taken  
23          for storage patients weren't advised that they were  
24          being stored for future testing. Do you remember,  
25          Professor Forbes, if patients were told, before

1 Dr Melbye carried out the testing on these samples?

2 A. I think that the answer would be probably not at that  
3 time. It's difficult to remember but this was very much  
4 a moving situation and the whole question of consent at  
5 that time was very woolly. Certainly later on it  
6 tightened up immensely and has changed even more since  
7 then. So I don't think that we would be asking for  
8 consent for storing samples but they might be told that  
9 they were being stored. So I'm very unclear as to when  
10 all these things happened.

11 Q. Yes. How would it have worked? How would the samples  
12 have got to Dr Melbye?

13 A. He actually came to Glasgow to pick them up and they  
14 were passed over to him in a frozen state.

15 Q. Yes. Who passed them over to him?

16 A. I'm sure it would be me.

17 Q. Yes. You said that patients were probably not asked for  
18 their permission to have them tested by Dr Melbye?

19 A. I think that is the situation. I don't think that at  
20 that time there was any concern about consent because we  
21 assumed that people would want to know about what was  
22 happening and what the implications of this new test  
23 would be. So I don't think that we asked for consent.

24 Q. Yes. Do you have any doubt about that,  
25 Professor Forbes?

1 A. I'm quite sure that we didn't ask at that time.

2 Q. Thank you. If we just read on in that paragraph,  
3 paragraph 9, you say:

4 "You ask specifically if consent and testing changed  
5 between 1984 and 1987 and the answer to that is of  
6 course it did. By 1987 specific consent was asked for.  
7 Often before that it was not. It was a gradual process  
8 which came in. I will go on to the next part, which is  
9 communication of results ..."

10 And so on. Could you explain to us what obtaining  
11 specific consent involved?

12 A. I think the important thing is that you are telling  
13 patients what is going to happen and why it's to happen  
14 and to ask their consent for it to happen. This was  
15 very much a change in the ethos of medicine. Until then  
16 the implication was that if you went to a doctor with  
17 a problem, he would do his best to find the cause of it,  
18 without asking your consent for blood samples or  
19 whatever, and that was how things were at that time.

20 I'm not saying that's the right thing because  
21 I think that now clearly it is not the right thing, and  
22 I think that before one does very much to people, there  
23 has to be implied consent and if you are doing anything  
24 invasive, like blood samples or endoscopy, you actually  
25 have to tell them exactly what are doing, what it will

1 find for them and what you can do about it, and that is  
2 implied consent and often is now written down and that  
3 is certainly safer.

4 Q. When you mention specific consent, does that involve  
5 obtaining consent before testing?

6 A. Well, I think it should be. I think it should be before  
7 testing. I don't think you can do a test and then say,  
8 "By the way, we have done the test and this is the  
9 result". So we have all changed our views in this.

10 Q. Yes. Thank you.

11 I would like to move away from the questions at the  
12 moment Professor Forbes and ask you to look at a bit of  
13 transcript from Dr Wilkie's evidence, which we heard  
14 yesterday. Could we go to page 13 of the transcript?  
15 Of course, Dr Wilkie is someone that you worked with at  
16 Glasgow Royal Infirmary?

17 A. Yes, indeed.

18 Q. That's right, isn't it?

19 A. And a very effective lady she was too.

20 Q. Yes. Well, at this bit of the transcript Dr Wilkie is  
21 talking about before she becomes involved in the project  
22 at the Royal Infirmary. If we look at line 23, I'm  
23 reading to her from her statement, she says:

24 "Dr Forbes had recently returned from a haemophilia  
25 conference in USA where it had been reported that

1 HTLV-III had been found in the blood of some patients  
2 with haemophilia ...

3 "'Dr Forbes had brought back some testing kits from  
4 the USA which were not yet licensed and which could test  
5 the presence of HTLV-III in the blood.'

6 "If we just stop there, Dr Wilkie, what is written  
7 there in that statement, that is your recollection based  
8 on your conversations with Dr Forbes at that time, is  
9 that right?"

10 She says, "Yes". So you see what Dr Wilkie is  
11 saying about the conversation that she remembers having  
12 with you, Professor Forbes?

13 A. Yes, I see it.

14 Q. Do you have any recollection of a conversation like  
15 that?

16 A. None whatsoever. It is very likely that it took place.  
17 I don't -- I certainly didn't bring anything back  
18 personally from the States in my hand but I am sure we  
19 had some connection in which tests were provided to us.  
20 Now, when this is, I'm not sure.

21 Q. Yes. Well, would it be before the Melbye testing?

22 A. I don't think so. The first we ever had available was  
23 the test that Dr Melbye produced. So I don't think this  
24 can be anything to do with the Melbye testing.

25 Q. Yes. So if Dr Wilkie thinks that you carried out

1 testing on two patients with an experimental test kit  
2 before the Melbye testing then she is wrong about that,  
3 is she?

4 A. Well, I certainly don't remember it. I don't think that  
5 could have happened because I wouldn't personally be  
6 able to do a test like that. I wouldn't think that is  
7 anything to do with me.

8 Q. We are jumping forward a little bit but just thinking  
9 about when you appointed Dr Wilkie to help with the  
10 project, did you at that stage know that you had 12  
11 patients which had tested positive?

12 A. I'm not sure. I don't remember the chronology of that  
13 but I knew that it was going to come that this epidemic  
14 would happen in Scottish haemophiliacs, as it did.

15 Q. Yes. Thank you.

16 Perhaps it might be time to have a short break, sir?

17 THE CHAIRMAN: Is that a suitable time?

18 MR GARDINER: Yes, sir.

19 THE CHAIRMAN: We will have a short break.

20 (3.10 pm)

21 (Short break)

22 (3.30 pm)

23 MR GARDINER: Professor Forbes, just before we broke, we  
24 were talking about a conversation that you had with  
25 Dr Wilkie. I wonder, do you think it's possible that

1 during that conversation with Dr Wilkie you were  
2 discussing the results of the Melbye testing?

3 A. I just can't remember any conversation like that. We  
4 discussed things every day, so we had communication all  
5 the time but I can't remember anything like that.

6 Q. Yes. The context is that, on Dr Wilkie's account, you  
7 have phoned her to ask her to become involved in this  
8 project and she describes you as agitated. I'm just  
9 wondering if a possible explanation for that, if  
10 Dr Wilkie is remembering it correctly, is that the tests  
11 that are being referred to are the Melbye tests. Do you  
12 think that's possible?

13 A. It could be. I just have no recollection.

14 Q. Okay. Thank you. I would like to ask you some more  
15 questions about the Melbye testing. You covered that in  
16 your supplementary statement, which is at [\[PEN0121328\]](#).

17 Your answer here is in response to a question --  
18 I think we should just have a quick look at that. It's  
19 in the schedule of our letter, which is page 2 of  
20 [\[PEN0120771\]](#).

21 The second paragraph. Question 2. We have touched  
22 on some of these things but just to deal with them all.  
23 The question is:

24 "The enclosed Lancet article, published on  
25 22 December 1984 and entitled 'HTLV III seropositivity

1 in European haemophiliacs', reported a study of 77  
2 haemophilia patients between December 1983  
3 and July 1984."

4 The questions are:

5 "Were the 77 patients different?"

6 We have looked at that:

7 "Were the 77 patients all being treated at the  
8 Glasgow haemophilia centre? What was the purpose of the  
9 study? What were the findings of the study? Were the  
10 patients aware that they were being studied? Was their  
11 consent obtained to be included in the study? Were the  
12 patients advised of the results of the study? Was  
13 consent obtained from the patients before publishing  
14 their data in the Lancet?"

15 I want to focus on that last question there,  
16 Professor Forbes, and you have answered it at  
17 paragraph 2.2 of your supplementary statement, where you  
18 say:

19 "There are some ... questions that you have asked  
20 which, to the best of my memory, I will try to answer.  
21 I am sure that the 77 patients in this study were in  
22 fact inclusive of the 19 patients that had already been  
23 looked at and whose samples were stored."

24 We have already looked at that. Then reading that  
25 short, you say:



1           "The purpose of the study was to try and find out  
2           how many patients in our whole population of patients  
3           were HIV positive, although of course we did not get  
4           every patient that we did look after. The patients were  
5           aware that we were undertaking further studies of the  
6           infection, although specific details were not spelt out  
7           to them. At that time it was not the policy of the unit  
8           to specifically get informed consent for each study that  
9           was carried out. The patients in the course of time  
10          were all told of the result, of what had been found. In  
11          particular those that were HIV positive were told and  
12          given specific instructions and counselling."

13           Then 2.3:

14           "Once again, at that time it was not the policy of  
15          the department to get specific consent from those who  
16          had been included in studies for the publication to be  
17          submitted to a medical journal. I don't think we have  
18          had any other publications."

19           So what I want to ask you, Professor Forbes, first  
20          of all, was who decided on the department's policy at  
21          that time, the policy about not getting specific consent  
22          for publication?

23          A. I don't think there was any committee but like all  
24          university departments, there was a hierarchy and mostly  
25          the administration of that was by consent, and I think

1           that in fact -- I'm not aware of any other studies  
2           requiring informed consent. So these things, of course,  
3           have changed and probably changed for the better, but  
4           that was the situation at that time.

5   Q.   So at that time the policy was not to ask patients'  
6        permission to use their data in medical publications, is  
7        that right?

8   A.   Yes. And that applied across the board, not just in HIV  
9        infection and so on.

10   Q.   Has the department's policy changed?

11   A.   Oh, I think so. I think that it would be fair to say  
12        that the whole area has changed and become much more  
13        open.

14   Q.   Yes, thank you. Thank you.

15            Could we go back to your original statement and  
16        questions now? I think we are on question 11.

17   A.   Yes.

18   Q.   The question was:

19            "What was Professor Forbes' practice in relation to  
20        telling his patients of positive test results? Did  
21        Professor Forbes inform his patients immediately upon  
22        receiving their results?"

23            I'll just read 12 because you deal with it in the  
24        same two paragraphs:

25            "What arrangements were made for patients to be told

1 of positive test results?"

2 Just looking at your statement, you answered those  
3 two questions at paragraph 10 and 11. Paragraph 10:

4 "We always had a very open policy about informing  
5 patients of the results. With regard to this particular  
6 test we did this in association with a session in which  
7 they were told the result but also told of the  
8 implications of what it meant as far as we knew at that  
9 time. The usual way this was done was to invite the  
10 patient to have a routine review to answer their  
11 questions, of which there were usually many, with the  
12 best information we had at that time."

13 In that paragraph, Professor Forbes, are you  
14 referring to the 12 patients who tested positive after  
15 testing by Dr Melbye?

16 A. Yes.

17 Q. Could you tell us a bit more how that was organised?

18 A. Well, it was a very emotional situation and we made  
19 a firm decision that we would tell the patients what had  
20 been found in the various tests that were done and the  
21 implications thereof. And this was done by asking them  
22 to come in, usually for a review. We could do it in  
23 private, confidential situation. They were told as best  
24 one can tell that kind of news to somebody, and then we  
25 tried to answer the questions, the myriad question that

1           arose from knowing that they were positive. And this we  
2           did as best possible with the information we had at that  
3           time.

4   Q.   Yes. So who would carry out that exercise,  
5           Professor Forbes?

6   A.   Well, usually myself.

7   Q.   Would you be on your own at that time with the patient?

8   A.   Usually. I am sure also that Dr Lowe who was getting  
9           more senior would also be involved in that. I'm sure  
10          when you ask him, he will certainly remember it. It's  
11          something you do not forget.

12  Q.   Yes. So it may not have been just you who did it?

13  A.   I think it wouldn't have been. I wasn't there  
14          100 per cent of the time and obviously some of them  
15          would be seen by Gordon Lowe.

16  Q.   Yes. Okay. If we just move on to paragraph 11. You  
17          say:

18                 "The samples were taken, sent off (after local  
19                 storage) to Dr Follett, and the results were then given  
20                 to the patients on a return appointment, usually a week  
21                 or two weeks thereafter."

22                 Presumably, with the Melbye testing, you wouldn't  
23                 need to do that?

24  A.   No, they all came back together as a single batch.

25  Q.   So it wouldn't be necessary to send the samples to

1 Dr Follett?

2 A. Well, we had the idea that we should follow up the  
3 positives, which we did, and that was done by  
4 Dr Follett.

5 Q. Yes.

6 A. So we wanted to confirm, using a slightly different  
7 test, that the answer was still the same and that they  
8 weren't forming antibodies and getting rid of the  
9 positivity.

10 Q. Yes. So was that done before the patient was told of  
11 their results?

12 A. No, we told them as soon as possible and we in fact had  
13 to make appointments for many of them especially and  
14 bring them in to tell them. We also tried at the same  
15 time to talk to their wives or partners.

16 Q. Yes. When we heard from Dr Wilkie, she said that  
17 sometimes she was given the responsibility of passing on  
18 the results of the tests. Does that accord with your  
19 recollection?

20 A. She would certainly be involved in that. I don't think  
21 she was ever given the responsibility solely of telling  
22 the patient.

23 Q. Thank you.

24 A. And the reason for that was not that we didn't trust her  
25 but so many other questions then arose and it was

1           probably better done with a group of people adding their  
2           penny's worth of information.

3    Q.   Yes.  Just thinking about the timing, Professor Forbes,  
4           when do you think the Melbye tests were carried out?

5    A.   Well, they must have been carried out before the  
6           publication date, which I have to remind myself of.

7    Q.   That's December 1984.

8    A.   Yes.  So before then or just before then.  Because there  
9           is always the delay in the writing of the paper.  It  
10           takes time.  And then the acceptance and publication.

11   Q.   Yes.

12   A.   So ...

13   Q.   Could we have --

14   A.   Up to some months before the date of the publication.

15   Q.   Perhaps we can date it with a meeting of haemophilia  
16           directors.  Could we look at [\[SNF0010255\]](#)?  You see,  
17           that's a meeting on 29 November 1984.  Can you see that?

18   A.   Yes, indeed, which I was there.

19   Q.   And you were there.  If you look at paragraph 4:  
20           "Dr Forbes described the findings relating to  
21           HTLV-III antibody seroconversion in a comparative study  
22           of haemophilia patients in Glasgow and Denmark.  This  
23           study would shortly be published in the Lancet."

24           So you must have had the results by that stage?

25   A.   Yes.  What's the date of this document?

1 Q. Well, the meeting is dated 29 November 1984.

2 A. So it must have been before that.

3 Q. Yes.

4 THE CHAIRMAN: What would have happened in between? From  
5 the point at which the paper was submitted, it would be  
6 reviewed by the editors and a decision sent back that it  
7 was available for publication or was to be published?

8 A. Yes.

9 THE CHAIRMAN: So that by November then, you knew that it  
10 was to appear in the Lancet.

11 A. Yes.

12 THE CHAIRMAN: So it had been accepted for publication?

13 A. Yes.

14 THE CHAIRMAN: How long would normally elapse between  
15 submission and that information, Professor Forbes?

16 A. It depends on the journal but it could be three months  
17 easily.

18 THE CHAIRMAN: And before that, because you have Dr Melbye  
19 involved, you will be sending drafts back and forward?

20 A. Absolutely.

21 MR GARDINER: I'm just trying to work out some dates here,  
22 Professor Forbes. Our information is that at this  
23 period the only tests for the virus were experimental  
24 ones. Dr Melbye was able to do testing. Dr Tedder was  
25 able to do testing. And it wasn't really until at least

1           1985, the beginning of 1985, that commercial tests were  
2           available to do the kind of tests that Dr Follett would  
3           have.

4   A.   Yes.

5   Q.   So doing the best we can -- and you seem to have the  
6           results here in November 1984 of the Melbye testing --  
7           can you help us with how the results would have been  
8           communicated to the patients?

9   A.   Well, we had a policy of openness with the patients and  
10          all of them would be requested to come in to keep an  
11          appointment to talk to us, and at that time the tests  
12          would be communicated, with as much information as we  
13          could give them at that time, which I don't think was  
14          all that much, but we would tell them that they were  
15          positive and what were the precautions, what to look out  
16          for, what the other conditions that they might present  
17          with. Opportunistic infections or opportunistic tumours  
18          as they are called.

19                So there was a lot of information to give the  
20          patients and about their lifestyle and the social  
21          situation. Also, if their wife or partner was there, we  
22          would take the opportunity of talking to her and that  
23          was, of course, where Patricia Wilkie came in  
24          eventually. She was very good at that.

25   Q.   Yes. You say eventually, just focusing on the first



1 testing, the Melbye testing, do you think that Dr Wilkie  
2 was involved in helping to pass on the results of that  
3 testing?

4 A. I find it very difficult to think back to just exactly  
5 what was happening at that time. But she had come to  
6 work with me in a different project on adult polycystic  
7 kidney disease, so she was certainly there or  
8 thereabouts during this time, and eventually I persuaded  
9 her to take on this additional commitment and it worked  
10 out very well from all points of view, because she was  
11 such a good counsellor and was able to talk to these  
12 patients and get from them a lot of information about  
13 their concerns and anxieties.

14 Q. Yes.

15 A. So that's how it worked. I'm just not sure of the time  
16 sequence exactly.

17 Q. Yes.

18 A. But it's not too far away so it might have been that she  
19 was involved.

20 Q. I see that we have still got the note of the meeting  
21 from November 1984 on the screen. I wonder if you could  
22 just look at paragraph 5:

23 "Dr Gibson reported the anxiety felt by parents of  
24 haemophiliac children treated at RHSC Glasgow,  
25 [\[Yorkhill\]](#), where imported Factor VIII had been used

1           until relatively recently. Five out of ten of these  
2           patients were HTLV-III antibody positive."

3           We have been trying to work out how that testing  
4           might have been done. Is it possible, Professor Forbes,  
5           that the Yorkhill samples could have been tested by  
6           Dr Melbye at the same time as your patients' samples?

7   A. Yes, I don't remember that, but who else would have done  
8           her testing, Dr Gibson's testing? I don't know.

9   Q. That's the question we have been asking.

10 A. Sorry, I don't know.

11 Q. Okay, thank you. I think I should also read -- although  
12           we have touched on it -- paragraph 13 of your statement,  
13           where you are addressing this question that we have been  
14           discussing: how the information was communicated.

15           Paragraph 13:

16           "It was at this time we employed  
17           Mrs Patricia Wilkie, who was a wonderful addition to our  
18           staff due to her long association with different  
19           counselling situations. Many other problems became  
20           apparent and we dealt with them on an ad hoc basis, in  
21           particular, the question of sexual partners and wives,  
22           and also the problem of children who had become  
23           positive -- although they were usually dealt with at  
24           Yorkhill. There is no doubt that a lot of time and  
25           effort was put into trying to do this correctly and

1 I think we were really quite successful."

2 Just moving on to the next question, which is  
3 question 14. This is a reference to the UK haemophilia  
4 reference centre directors' meeting on 10 December 1984.  
5 I think, professor, you should now have a copy of the  
6 minutes of that meeting. That's [\[SNF0013850\]](#).

7 A. Yes, I have a copy in my hand.

8 Q. We will just get it on the screen. We see that this is  
9 minutes of a meeting, 10 December 1984, at Elstree and  
10 we see present Professor Bloom, Dr Kernoff, Dr Cash,  
11 Dr Craske are some people that were included. We see  
12 that you also attended that meeting?

13 A. Yes.

14 Q. Dr Rizza, Dr Savidge, Dr Tedder. Do you remember that  
15 meeting?

16 A. No, but I was clearly there.

17 Q. Well, the reason I have referred to it is that it seems,  
18 if we look at page 3853, which is the fourth page in,  
19 you see the second paragraph from the bottom, the  
20 paragraph that begins "a long discussion"?

21 A. Yes.

22 Q. "A long discussion took place on whether persons found  
23 to be positive were to be informed. Several differing  
24 views were expressed. It was agreed that each clinician  
25 would decide for each case, depending on the facts of

1 the case but in general to provide information if asked  
2 for."

3 So we see that this is a topic that is being  
4 discussed. If we go over the page to page 5, 3854,  
5 after this discussion, the middle of the page there is  
6 a paragraph that begins "the Chairman". So  
7 Professor Bloom:

8 "... summarised by saying that testing should be  
9 instituted as soon as possible, and that information on  
10 the test results should not be given automatically but  
11 if asked for. HT material should be given  
12 preferentially in those cases where concentrate is  
13 required ..."

14 And so on. So we see there that there is the  
15 discussion and that the chairman is summarising that  
16 results should not be given automatically. It seems  
17 that it is to be left to the discretion of the clinician  
18 to a certain extent whether results are passed on. Do  
19 you have any memory of that discussion at all,  
20 Professor Forbes?

21 A. I have memory of great differences of opinion, where  
22 some people were saying, "definitely not" and some  
23 people said, "It's only fair to tell them". And  
24 I personally took the view that it was only fair to tell  
25 people and that there was no way of avoiding the telling

1 of bad news and that was our policy. But I know that  
2 some people didn't tell their patients at that time.

3 Q. Why did you think that? What was your reason for coming  
4 to that view?

5 A. Well, no matter what, the bad news was going to be there  
6 at some time. We didn't understand fully what the  
7 implications were but we suspected from what we knew  
8 already about the natural history of the disease that  
9 these patients were being given almost a death sentence,  
10 because most of them in fact up until that time, the  
11 ones who were diagnosed with positive antibodies, died,  
12 and died quite quickly thereafter, within the year. So  
13 we felt that it was only fair to them and their families  
14 to know what it was all about. But, as I say, it was  
15 a very divided view.

16 Q. Did the communication of the results have any  
17 implications for the treatment that you could offer the  
18 patients?

19 A. Well, there was virtually no treatment at all at that  
20 time and you have heard of the successful introduction  
21 of different drugs over the years but what we heard  
22 today was mainly 10/15 years further down the line, when  
23 drugs became available. When we started out, there was  
24 virtually nothing that was going to be effective.

25 Q. Yes. Just looking at the next question, did your

1 practice about informing patients of positive test  
2 results change between 1984 and 1987?

3 A. I don't think it changed between these dates. We had  
4 a very open policy and tried our best to be as up front  
5 as possible. So it didn't change. It was always there.

6 Q. Was there a point where pre-test counselling was  
7 introduced?

8 A. I think that would be the norm nowadays, that to get  
9 consent you have to tell them what you are going to do  
10 and why you are doing it and what the implications are.  
11 So I think pre-test counselling is very much a more  
12 recent addition.

13 Q. Yes. Where would that date from, would you think?

14 A. I think it would be well into the end of the 1980s/the  
15 beginning of the 1990s.

16 Q. Yes.

17 A. By that time we had a better idea of what might be done  
18 for the patients and what drugs would be available and  
19 what effect they would have, and also about the spread  
20 of disease, particularly to other family members and so  
21 on. So it's a different situation.

22 Q. Yes. Thank you.

23 Just moving on to the next topic, which is going to  
24 be one of our last, this is all to do with a meeting of  
25 haemophilia patients in Edinburgh, and we have it as

1 19 December 1984. If we look first at the questions,  
2 questions 16, right through to the end, are all about  
3 what happened at the meeting, what happened before the  
4 meeting and so on. I think you answer them in your  
5 paragraphs 14 to 19. Just looking at paragraph 14, the  
6 question you are addressing here, first of all, is: what  
7 was the purpose of the meeting on 19 December 1984? You  
8 say:

9 "I think some of these questions probably should be  
10 asked of Dr Ludlam, who organised the meeting in  
11 Edinburgh on 19 December 1984. It was to inform a group  
12 of patients from Edinburgh about what was happening with  
13 the virus and the implications thereof. I really don't  
14 know why I was invited to go but I was, and invited to  
15 chair the meeting."

16 Just pausing there, Professor Forbes, are you able  
17 to say now why you were invited to go?

18 A. Well, we have had a lot of discussion about my failing  
19 memory and clearly I went with a view to chairing the  
20 meeting and to do that happily. I had thought in  
21 retrospect that it was only Edinburgh patients but my  
22 colleagues tell me that in fact it was a general  
23 invitation to patients to come to the meeting, which was  
24 in Edinburgh, and organised by Dr Ludlam.

25 So I am afraid that I have a major blank in some

1 parts of this but I do remember the meeting and  
2 I remember the people who were there, and it was Chris  
3 Ludlam who was the speaker for Edinburgh and  
4 Brian McClelland from blood transfusion, and there was  
5 a social worker as well, who I think you are going to  
6 hear tomorrow. So I have a blank about parts of it but  
7 I do remember some of it and it was a general discussion  
8 to try and educate the patients and their families, who  
9 came along, about what might or might not be done and  
10 what was available by way of treatment and what was  
11 available to help them cope with all the different  
12 problems that are now arising.

13 So it was very much an educational-type meeting,  
14 held in Edinburgh.

15 Q. Yes. Well, I would like to you be careful,  
16 Professor Forbes, to tell us what you can remember and  
17 not what you may -- how shall I put it?

18 A. Have learnt.

19 Q. Have learnt. If you can try to be careful about that.  
20 Do you remember what discussions you had before the  
21 meeting?

22 A. I don't think we had any discussions from my defective  
23 memory. I don't think -- there was no agenda set and  
24 there was nothing that we were told not to say or to  
25 say. So it was just an open meeting.



1 Q. Yes. How many people do you think attended?

2 A. Well, I remember the lecture theatre being pretty full  
3 and I have no idea how many people but I'm since told  
4 that it holds up to 200 but I don't think there were 200  
5 people there. But less than that. But it was pretty  
6 full.

7 Q. You have put 20 people there, so that sounds more. What  
8 you are telling us now is more than 20?

9 A. Yes, I'm being persuaded. So I have to be careful what  
10 I'm saying. I thought from memory it was about 20  
11 people but there we are.

12 Q. If we can try to stick to your memory, Professor Forbes.

13 A. Yes, sorry.

14 Q. And your memory, is it still telling you 20 people?

15 A. Well, I just remember the few people in front that  
16 certainly asked questions, and I didn't think it was as  
17 many as I'm now being informed about. So 20 people may  
18 be wrong.

19 Q. Yes. Do you remember who spoke first?

20 A. Yes, Chris Ludlam.

21 Q. And can you remember broadly what he told the meeting?

22 A. I have no recollection of anything he spoke about, but  
23 it was all relevant to the background information on  
24 this new virus.

25 Q. Yes. Was it more specific than a new virus, can you

1 remember?

2 A. I don't remember anything that was more specific but --

3 you must remember that many of the people in the

4 audience had already read about this from the media and

5 newspapers and so on. So I'm not sure that he was

6 telling them anything particularly new.

7 Q. You say here at paragraph 17 that you think the meeting

8 went on for about two hours?

9 A. I think about two hours. I remember quite clearly going

10 home on the train after it and it was dark. So it would

11 be about two hours, I would have thought.

12 Q. When do you think it started?

13 A. About 7 o'clock. It was in the evening.

14 Q. Paragraph 18. You say:

15 "I see from the note that Dr McClelland (who was

16 from BTS) was there but I don't remember what any of

17 them said."

18 When you say "the note", what note are you referring

19 to there?

20 A. I think that was something that you had sent. One of

21 the questions maybe that you had asked.

22 Q. Yes.

23 THE CHAIRMAN: 21.

24 MR GARDINER: Yes, question 21, thank you. You say:

25 "From memory I believed that patients had been told

1 about the tests that were done but I don't remember if  
2 any of the people at the meeting had not been tested and  
3 subsequently wanted to be tested. Most of the patients  
4 seemed to know what kind of treatment they had been on  
5 and I don't remember that as a particular point of  
6 discussion."

7 You seem to be describing something a bit more  
8 specific than just a general concern about a new virus?

9 A. Oh -- and how they might have been exposed to the virus.  
10 That would be the question of treatment.

11 Q. Yes. Do you remember what the people that came were  
12 told about the possibility of having been exposed to the  
13 virus?

14 A. I think they were told that some of them had been  
15 exposed but there was no particular test available at  
16 that time, but that was coming on stream and that in the  
17 course of time they would in fact have communication, if  
18 they wished it, from their haemophilia director. So it  
19 was very early days.

20 Q. So communication, if they wished it from their  
21 haemophilia director. Do you have a recollection, as  
22 you are sitting there, Professor Forbes, of those words  
23 being said at the meeting?

24 A. I have no recollection of any words that were said at  
25 the meeting but that would be the implication, that they

1           would be told in the course of time if there were any  
2           further tests, or if they wanted further information,  
3           they could come and ask about it. But I have to say  
4           that my memory is very hazy about this although  
5           I certainly do remember going home from the meeting.

6    Q.   Yes. But you are telling us that you have a memory of  
7           that message being imparted, that --

8    A.   That, I think, is right. I don't remember what words  
9           were said.

10   Q.   Thank you. Then just reading on, paragraph 19:

11                 "The patients were quite generally well-informed.  
12           They were not particularly told that HTLV-III could be  
13           a terminal illness although many of them knew of  
14           patients who had died, particularly in America. As far  
15           as I know, there was no discussion about Scottish blood  
16           products as opposed to American blood products. In  
17           particular I can remember the mood of the meeting and  
18           I certainly don't remember any hostility from the  
19           audience."

20                 You have a personal recollection of that,  
21           Professor Forbes, do you?

22   A.   I have a memory that there was no hostility shown at all  
23           and one would have thought that there might have been  
24           but I'm not aware of it.

25   Q.   You say:

1            "I think they were generally shell-shocked at the  
2 information that had been given to them."

3            How did you come to form that view?

4 A. Well, the audience became very quiet at some points and  
5 that would be an implication that they were digesting  
6 what they had been told about what was happening, but  
7 I have no recollection of any hostility towards anyone  
8 at all.

9 Q. Yes. (Pause).

10           Professor Forbes, can you remember if anybody else  
11 spoke to the meeting apart from Dr Ludlam?

12 A. I know that Dr McClelland was scheduled to speak and I'm  
13 sure he did but I don't remember the detail of what he  
14 said, but I don't remember anyone else speaking. But  
15 there was a general question and answer session so no  
16 doubt others did speak.

17 Q. Yes. These were questions from --

18 A. From the audience.

19 Q. Can you remember what sort of questions were being  
20 asked?

21 A. I don't remember any specific questions but they were  
22 very general information-seeking questions.

23 Q. Yes. Thank you.

24            Sir, I propose to leave that now unless ...

25 THE CHAIRMAN: I'm still in some state of confusion over the

1 timing of the Melbye exercise.

2 You gave me earlier an indication, professor, of the  
3 sort of timing that could be involved when an article  
4 was submitted and reviewed and eventually published;  
5 which if it had applied in this case would have thrown  
6 one back several months into 1984.

7 If we look at the internal information, it might  
8 suggest that in this case the process was very much  
9 faster. So would you like to look at it with me,  
10 please, and see why I'm saying that?

11 A. I should just add that the Lancet often had a more rapid  
12 publication schedule than other journals. They may  
13 actually give dates on that paper, when it was first  
14 submitted.

15 THE CHAIRMAN: It doesn't. I have looked for that.

16 A. Okay.

17 THE CHAIRMAN: But there are two bits of information in it  
18 that may bear on this particular point.

19 I think we have it anyway. Can we look at the  
20 second page, please. [\[LIT0011702\]](#).

21 If you look at the top of the left-hand column it  
22 states in the first place that blood was taken in  
23 Glasgow between December 1983 and July 1984.

24 So July 1984 is clearly in the frame. But if we look at  
25 the end of the paragraph headed "Results", we see that

1           it's narrated that a Scottish patient died  
2           in late October 1984. Have you found that?

3    A. Yes, yes.

4    THE CHAIRMAN: Do these dates help at all in giving  
5           a reference point for the Melbye study?

6    A. No, I think with regard to the second point, you say the  
7           death of a patient, I think that would be added in the  
8           text and probably is not relevant particularly to the  
9           actual study and the samples and so on. But it helps to  
10          date it from some point. So at least that was in the  
11          text that went to the editor of the Lancet.

12   THE CHAIRMAN: But the study itself could have been  
13          somewhere after July.

14   A. Yes.

15   THE CHAIRMAN: And possibly soon after July.

16   A. Yes.

17   THE CHAIRMAN: Possibly in July? That's one point in the  
18          article. The other is the impact that the information  
19          about the tests may have had on you because, one way or  
20          another, by this date, and therefore before  
21          the December 1984 meeting, it was known that a Scottish  
22          Haemophilia A patient had died of AIDS. Was that not  
23          a factor that might have caused you to be somewhat  
24          disconcerted?

25   A. Well, any death is disconcerting and certainly that does

1 put a date. But, of course, the samples from that  
2 patient may have been tested and tested some months  
3 before for the study.

4 THE CHAIRMAN: We know it was May and July, at least the  
5 samples are measured as at May and July of 1984, just  
6 above the death.

7 A. Yes.

8 THE CHAIRMAN: So he was being studied in the same period,  
9 but it doesn't help you beyond that?

10 A. No, I don't think so.

11 THE CHAIRMAN: Thank you.

12 MR GARDINER: I just have one article I would like the  
13 professor to look at, sir.

14 Could we have [\[LIT0010829\]](#)? You don't have a hard  
15 copy of this, professor.

16 A. No.

17 Q. If you could see that, it's an article from the Scottish  
18 Medical Journal, "Acquired Immune Deficiency Syndrome --  
19 an overview."

20 You will see volume 30, January 1985, number 1. If  
21 we could go to 0834, we see in the middle of the page  
22 there that this is an article that you have written,  
23 together with JA Gracie, Karin Froebel, R Madhok,  
24 Professor Lowe. Does it ring any bells with you,  
25 Professor Forbes?



1 A. Oh, yes, I remember writing it.

2 Q. Yes, thank you. Could we have a look at page 5, which  
3 is 0833? The left-hand column, about two thirds of the  
4 way down, the sentence that starts "The one haemophiliac  
5 ..." which is a bit further up, actually. That's it,  
6 thank you. So just reading there:

7 "The one haemophiliac who has died of AIDS in  
8 Scotland received a large amount of commercial  
9 Factor VIII from the USA whilst being treated in  
10 England. The implications are that in Scotland the AIDS  
11 virus does not seem to have affected the donor pool as  
12 yet but a test for HTLV-III virus antigen, which should  
13 be available soon, will be valuable in screening for  
14 virus contamination."

15 Professor Forbes, this is an article which appears  
16 in 1985 and it must have been available for revision  
17 quite close to the publication date, and we are  
18 wondering how that statement has come to be made in this  
19 article, given what we have heard about patients being  
20 infected earlier than this.

21 A. I'm not quite sure that I understand the point you are  
22 making. Could you go back over it?

23 Q. Well, the statement is:

24 "The implications are that in Scotland the AIDS  
25 virus does not seem to have affected the donor pool as

1 yet but a test for HTLV-III virus antigen, which should  
2 be available soon, will be valuable in screening ..."

3 We know that by this stage the AIDS virus has  
4 affected the donor pool in Scotland.

5 A. Well, I think my understanding from this is that we  
6 thought that the contaminated batch of Factor VIII had  
7 been given when he was in England.

8 Q. I'm thinking of the implicated batch which was  
9 responsible for infecting the Edinburgh cohort?

10 A. Oh.

11 Q. Of course that was what the meeting in December 1984 was  
12 about.

13 A. But there was no doubt that it was inevitable that the  
14 donor pool in the United Kingdom was going to be  
15 affected as the disease was brought into the UK, and  
16 that people who were HTLV positive were going to be  
17 giving blood at some stage. So that's almost a logical  
18 sequelae of what we thought would happen.

19 THE CHAIRMAN: Professor, were you the editor of this  
20 journal at some stage?

21 A. Yes.

22 THE CHAIRMAN: At this time?

23 A. Yes.

24 MR GARDINER: So, Professor Forbes, if you remember,  
25 I showed you the minutes of the meeting

1 from November 1984.

2 A. Yes.

3 Q. Perhaps we can have them up again. [\[SNF0010255\]](#). Can we  
4 have a look at paragraph 3? Can you see that?

5 A. Yes.

6 Q. "Dr Ludlam explained the circumstances in which it had  
7 been discovered that 16 haemophilia patients treated  
8 exclusively with SNBTS Factor VIII had developed  
9 antibodies to HTLV-III, leading to the presumption that  
10 a Scottish plasma pool had been contaminated by a donor  
11 carrying HTLV-III. Various aspects of the  
12 epidemiological, pathological and ethical problems were  
13 discussed."

14 So that seems to be Dr Ludlam reporting that the  
15 AIDS virus has affected the Scottish blood donor pool,  
16 does it not?

17 A. Yes, indeed.

18 Q. So that's the purpose of our question about this  
19 article. We were wondering how that statement had found  
20 its way in.

21 A. Well, I'm not sure when the article was written but it  
22 would certainly be before the date of the publication,  
23 probably a month before. So when I wrote it, I don't  
24 think I had either been at this meeting or this had not  
25 impinged on my conscious level.

1 Q. Yes.

2 A. So it certainly was the beginning of the anxiety about  
3 contamination of the donor pool.

4 Q. Yes. Well, Professor Forbes, just for completeness, as  
5 we lawyers say, if we go up to the top of that page, we  
6 see, just to remind you, you were at that meeting.

7 A. I admit that fully.

8 Q. Sir, I don't have any more questions for  
9 Professor Forbes?

10 THE CHAIRMAN: Thank you.

11 MR GARDINER: Thank you very much, Professor Forbes.

12 THE CHAIRMAN: Mr Di Rollo?

13 Questions by MR DI ROLLO

14 MR DI ROLLO: Yes, sir, thank you.

15 Can I ask you about the December 1984 meeting first  
16 of all? One of the things that you have indicated in  
17 your evidence today is that you have obviously discussed  
18 this before coming to give evidence today with  
19 colleagues. Is that right?

20 A. Yes.

21 Q. Who have you discussed it with?

22 A. Mainly with Gordon Lowe.

23 Q. And who else?

24 A. With Chris Ludlam.

25 Q. Right.

1 A. Who was there. And I think these are the only two  
2 people I have actually met up with.

3 Q. When did you discuss it with Dr Ludlam?

4 A. It was after the last time I was here, which is maybe  
5 a month ago.

6 Q. Right.

7 A. Because I was surprised at what I had heard about the  
8 meeting, that it was in fact a meeting, and indeed my  
9 colleagues in Glasgow said that it was a meeting for the  
10 whole of Scotland. But I had thought it was only  
11 a meeting for the Edinburgh patients.

12 Q. How long did you discuss it for with Dr Ludlam?

13 A. How long?

14 Q. Yes. How long did you have a discussion about this  
15 meeting?

16 A. I think we were talking over lunch.

17 Q. Did Dr Ludlam indicate what his recollection of matters  
18 was in the course of that discussion?

19 A. He was clearly of the impression that it was a meeting  
20 which was attended by Glasgow as well as other  
21 haemophiliacs round the country. And he also said that  
22 I must have remembered that or should have remembered  
23 that, but I certainly didn't.

24 Q. Do you remember that? You didn't remember it when you  
25 had your discussion with Dr Ludlam. Do you remember

1           that now?

2    A.  No, I still don't remember it now but Dr Lowe had said  
3           that we had in fact written, as a result of the meeting,  
4           to various patients in the West of Scotland and that  
5           I had written the letter to them.  So it may be true.  
6           It's just defective memory, I'm sorry.

7    Q.  Let's just have a look at that.  Did you have  
8           a discussion with Professor Lowe after you discussed it  
9           with Dr Ludlam, this meeting?  In other words having  
10          spoken to Dr Ludlam --

11   A.  I think he was at lunch with us.  I think we were all  
12          discussing it together.  They were amazed that I had not  
13          remembered so much of what went on.

14   Q.  Professor Lowe wasn't at the meeting at Edinburgh in  
15          1984.

16   A.  I think that would be before his time.

17   Q.  Right.  And whether or not you wrote to patients after  
18          the meeting isn't really relevant to the actual meeting  
19          itself and who was at the meeting.  Is that not fair?

20   A.  I think that we were reporting back to the generality of  
21          patients.

22   Q.  Right.

23   A.  That's my understanding of what I'm told.

24   Q.  Have you ever seen a letter to that effect?

25   A.  No.  There must have been a letter and it must have gone

1 out.

2 Q. Can we just concentrate then on your recollection of the  
3 meeting at Edinburgh, because we are not really going to  
4 get very far if we think about what other people's  
5 recollections are?

6 A. Okay.

7 Q. Your statement to the Inquiry, which we have seen, and  
8 your original recollection, it doesn't appear that there  
9 was anybody from Glasgow, ie, Glasgow patients, at that  
10 meeting in Edinburgh. Is that correct?

11 A. Well, that was my recollection.

12 Q. Yes. That there were no Glasgow patients?

13 A. That's what I think.

14 Q. Right. In your statement you say there were about 20  
15 people or so at the meeting other than the doctors that  
16 were present. Is that correct?

17 A. Well, that's what I thought and shows how defective  
18 memory can be.

19 Q. Your memory may be perfectly accurate. Why is it  
20 defective?

21 A. I would have said my memory is not wonderful nowadays.  
22 But that is what I said and that's what I thought at the  
23 time.

24 Q. All right. Are you saying that you don't actually now  
25 have any understanding of why the meeting was held?

1 A. My understanding was it was an educational exercise for  
2 patients in Edinburgh.

3 Q. Do you recall whether it had any link to what we saw  
4 there in the document that was put before you about what  
5 Dr Ludlam had discovered in relation to his patients?

6 A. I have no recollection of that at all and that certainly  
7 didn't come out at the meeting, as I remember.

8 Q. Do you know why you were invited to go to the meeting?

9 A. I have no idea but I had known Dr Ludlam for a long time  
10 and it seemed reasonable to have a neutral person at it,  
11 as I saw.

12 Q. In the minutes of the meeting we just saw, we noticed  
13 there that there is mention of discussion of ethical  
14 problems. This is the November meeting that we saw just  
15 now that you said you were at. What were the ethical  
16 problems in relation to what had occurred? Do you know?

17 A. I don't think it was anything to do with the meeting  
18 that was held in Edinburgh. I'm not aware of any  
19 ethical problems arising from that.

20 Q. I'm referring, I think, to the ethical problems that  
21 might arise as a result of the fact that patients had  
22 been tested without their knowledge and the tests had  
23 been proved to be positive, and whether any ethical  
24 problems would arise as a result of that.

25 A. Well, I don't think in these days that there was any



1 ethical dilemma at that time, and it certainly wasn't  
2 perceived by the people involved at that time.

3 Q. You say that, Dr Forbes, but Patricia Wilkie told us  
4 yesterday that you had originally carried out tests on  
5 a non-named-patient basis and that when one or two of  
6 them had proved to be positive, you decided to stop and  
7 you were concerned about that and she said that you  
8 stopped testing for ethical reasons. Now is she wrong  
9 about that?

10 A. Well, I don't remember that happening but certainly we  
11 were appalled when we found that some of our patients  
12 were HTLV-III positive. That was a devastating time in  
13 one's life, that this virus had crept in to our  
14 patients.

15 Q. When you sent samples for testing originally, did you do  
16 so on a named or on an anonymous basis?

17 A. The samples were all labelled. So they were not  
18 anonymous. They were, therefore -- I think, it is  
19 important to say that there was action required to be  
20 taken when they were found to be positive.

21 Q. Right.

22 A. And we could identify the people who were involved, and  
23 we told them.

24 Q. Right. So as soon as you discovered the outcome of  
25 these tests, you took steps immediately to inform them

1 all of the results?

2 A. Yes, all of them.

3 Q. Why did you do that?

4 A. On a personal basis. Well, I think it was important.

5 We were going to tell them very bad news. There were

6 implications not just for them but for their families

7 and their lifestyle, and it was to my mind very

8 important that we tell them what had happened. Nothing

9 was being hidden away.

10 Q. Did you understand that, in December 1984, a similar

11 thing had occurred at Edinburgh, in that tests had been

12 carried out and that specific individuals were

13 identified or known to be HTLV-III positive, and that

14 was the purpose of the meeting or one of the purposes of

15 the meeting in December, to tell the patients of that

16 fact? Was that what you understood was going to happen?

17 A. I don't think I knew that at the time.

18 Q. I see.

19 A. But I think it was about that time that in fact the

20 patients were told what had happened.

21 Q. Was it your view that patients should have been told

22 then the outcome of any tests that had been carried out

23 on them?

24 A. Well, I think they were very soon after or as soon as

25 possible thereafter.

1 Q. That's what your patients were told?

2 A. Yes.

3 Q. Were your patients told before the article was published  
4 in the Lancet?

5 A. I can't remember the chronology. We had a policy of  
6 writing to them when they had a positive test and  
7 inviting them to come in for a discussion and that was  
8 when they were told.

9 Q. So I think the question was whether or not you would  
10 have told your patients before the article was  
11 published. Are you able to help on that?

12 A. We would start to do the process of telling the people,  
13 and that takes many weeks. So whether the article was  
14 published or not, I can't say now, but the process of  
15 telling them had started.

16 Q. Sir, I don't think there are any other questions that  
17 are going to elicit any useful evidence.

18 THE CHAIRMAN: Yes. Mr Di Rollo asked you a question.  
19 I don't think you answered directly, professor. It was:  
20 was it your view that patients should have been told the  
21 outcome of any tests that had been carried out on them  
22 and your answer was, "Well, we did tell them," but  
23 I think that the question was directed towards what  
24 motivated the telling rather than the telling. Did you  
25 think that they ought to be told?

1 A. Well, I'm not sure that I really understand the subtly  
2 of your point.

3 THE CHAIRMAN: Well, it's the difference between just doing  
4 something casually and doing something as in implement  
5 of an obligation that you felt.

6 A. We did feel an obligation and the positivity was  
7 devastating to us but also to the patients and to -- we  
8 felt an obligation to tell them as best possible what  
9 the implications of the test for their routine lives and  
10 their way of life and for their families and so on. So  
11 we did feel an obligation, and as rapidly as possible  
12 that was done.

13 THE CHAIRMAN: Was Dr Wilkie involved in that?

14 A. Eventually. I'm not sure just exactly when she came  
15 into post but she was certainly involved latterly, very  
16 deeply involved, in telling patients in association with  
17 all the other helpers who were there.

18 THE CHAIRMAN: "Headhunting" is a particular expression in  
19 current parlance. Had you really sought her out to get  
20 her help for this purpose?

21 A. Well, it was fortuitous because she was already working  
22 with us on something which she was very expert in, which  
23 was the genetic counselling of various things, of which  
24 part of it was genetic counselling of haemophilia. But  
25 her employer at that time was to do with adult

1 polycystic kidney disease. And she was there in post  
2 and agreed to do the other part of the job, which  
3 I think became much more important to her and to us.

4 THE CHAIRMAN: Mr Anderson? Mr Sheldon?

5 I have only one further matter to ask you to look at  
6 and that is a quotation on page 3 of [\[LIT0011702\]](#).

7 I imagine it just comes fortuitously at the end of the  
8 article that we have been looking at. Have you read it?

9 "'Viewing medicine as a battle too often reduces the  
10 patient to an object -- a fragile boat, a rudderless  
11 frigate, a hapless barge of statistical misfortune  
12 tossed upon the stormy seas of illness. A doctor, in  
13 turn, views his responsibilities as a naval skirmish --  
14 a confrontation to be prepared for, fought, and won.  
15 The patient in this perspective is entirely passive. He  
16 hopes only to be saved. The doctor sends in his armada  
17 and tries to occupy disease's strategic islands; or  
18 occasionally he has to retreat. What he does not do is  
19 relate well to his patient. The family of the patient  
20 is also relegated to the role of helpless bystander ...  
21 with distressing regularity, families are excluded from  
22 any substantive involvement with the physician ... they  
23 hover compliantly in the background while physicians,  
24 medicine's gladiators, unsheathe their swords and do  
25 battle with disease. What a waste of powerful, and

1 potentially healing, resources!'"

2 The language might not be yours but is that a proper  
3 characterisation of the paternalistic attitude of the  
4 period?

5 A. I think it's a splendid quotation.

6 THE CHAIRMAN: Thank you.

7 We will adjourn.

8 (4.40 pm)

9 (The Inquiry adjourned until 9.30 am the following day)

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