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.

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

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

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

(9.39 am)

(Short adjournment)

(9.55 am)

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

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

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

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

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

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

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

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

MS PATRICK: Thank you, sir.

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

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

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

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

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

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

From now on these things will not be done by

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

So --

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

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

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

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

MR DI ROLLO: Thank you.

THE CHAIRMAN: Very well.

PROFESSOR CLIFFORD LEEN (sworn)

Questions by MS PATRICK

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

A. Yes, I do.

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

A. Yes.

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

A. Yes.

Q. Can you tell us about that association?

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

Q. Okay.

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

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

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

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

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

A. I was, yes.

Q. What did your work there involve?

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

Q. So it didn't go exactly the way you planned when you first arrived there?
A. No.
Q. Then we can see that you were a senior registrar in Manchester and spent time there -- if we go over the page -- and in London, before returning to Edinburgh in May 1989?
A. Yes, it is.
Q. You then became a consultant physician of HIV Infectious Diseases initially at City Hospital and then at the Western General Hospital?
A. The hospital closed down and we moved the unit to the Western.
Q. When was that that it closed?
A. That was in 1998, the summer of 1998.
Q. Then if we return to page 3, you tell us about your current position, which is still consultant physician in infectious diseases and now honorary professor in the department of medicine at the University of Edinburgh. You treat community-acquired and hospital-acquired infections and have a special interest in blood-borne viruses, and you tell us that you are the lead clinician for blood-borne viruses in the unit.
A. Yes.
Q. Do you mainly see patients with HIV?

A. I do, yes. I treat them as well.
Q. Yes. Does that make up the greatest proportion of your patients?
A. It is probably coming to about 50 per cent of my workload in terms of time that I have spent caring for patients.
Q. So how long have you been treating patients with HIV?
A. Since 1986, when I started as a senior registrar in Manchester. The first day I started there in January, I was asked to help look after a patient with AIDS. That was interesting.
Q. You tell us about that further down page 3. Did that start your interest in the condition?
A. No, my interest was before that. I heard about HIV and AIDS certainly -- not so much about HIV but about AIDS initially. In actual fact, it's like 30 years since the first case of AIDS was reported in the literature. And it was the ultimate challenge for any infectious disease doctor because there you have a patient whose immune system is decimated by something, obviously HIV, and the challenge was to treat all the infections which arise as a result of this diminished immune system. That was the challenge.
Q. Yes.
A. Obviously the ultimate challenge was to find treatment

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

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

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

Q. Over the page --

A. I apologise for that.

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

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

are mostly HIV-related?

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

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

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

Q. Right.

A. That's a long time ago.

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

A. Yes.

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

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

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

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

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

A. Yes.

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

A. Yes.

Q. Thank you.

I would like to refer you now to your report, which is [PEN0121044], firstly to page 2, basically to the second paragraph there.

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

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

Q. Yes. That conference was in 1990?
A. Yes. It was in the USA.
Q. When you say the "first consensus statement", what do you mean by that?
A. I think, before this drug was licensed, there were some studies on this drug. There was no other treatment for HIV, so when the drug first came, the first question was: how best do we use the drug? Should we use it in everyone with AIDS? The answer is probably yes. And then what about those people who are HIV positive but haven't developed AIDS?

So this would be to look at how to best use this drug. That was set up by the Americans to try and have a group of experts and have their views on how best to do them. That was the first real meeting of people working in the field to try and formulate, sort of recommendations, sort of guidelines type of things.
Q. Would that have been followed in the UK?
A. Not necessarily but those people in the know would probably want to see what views were expressed and then use their own judgment as to which bit to follow.
Q. Yes. You tell us there that the panel there concluded that a large proportion of the asymptomatic and mildly symptomatic HIV-effected population were candidates for early therapy with Zidovudine.

A. Yes.
Q. Then you tell us further down the page that the first British consensus on the treatment of HIV appeared in April 1997 in the Lancet, and thereafter was quickly revised and British guidelines were then produced from 2000 onwards. Before that time, were there any consensus statements or guidelines in Britain that clinicians could follow?
A. None at all. Between sort of 1990 to 1996 there was lots of activity, looking at finding candidate drugs which might be useful.
Q. Yes.
A. There was a lot of knowledge arising as well in terms of how to look at the progression of HIV, predictors of progression, and also there was a new technology which was being used in the labs, which was looking at measuring the amount of virus there is in the blood.

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

So the founding chair of the British HIV

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

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

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

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

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

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

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

So that was straightforward. What was more difficult and less straightforward was: should you use the only drug you had in those patients who are infected but showing no signs of disease or of any HIV related problems? That was the big debate, and we knew that was an important issue because the benefit we got from using Zidovudine alone in AIDS patients was limited. So it was one bullet you had. When is it best to use that bullet? That was the dilemma that all clinicians had at the time.
Q. Yes. You tell us in the first paragraph that we are looking at here that in the early 1980s, when an HIV-infected patient was diagnosed, this patient may well have been cared for by the physician who made the initial diagnosis, so there were various different types

of doctors treating the virus at that time?

A. Quite likely, yes.

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

A. It would be, yes.

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

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

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

Q. Yes.

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

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

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

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

Q. But there weren't any guidelines then?

A. There weren't any guidelines.

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

A. Diagnosed the patient's conditions, yes.

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

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

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

a patient with haemophilia coming to the infectious diseases unit.

A. Yes.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

A. Yes.

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

A. Very much so.

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

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

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

A. For patients with AIDS, late stage disease, yes.
Q. Was that any different if the patient had not yet acquired AIDS?
A. I think the benefit will wane over time and the reason is that the HIV virus is a very dynamic virus, which replicates very much. It is thought that up to 2 billion copies of the virus is actually produced every day. A huge turnover.

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

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

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

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

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

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

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

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

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

A. DDI.

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

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

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

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

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

A. It would be early 1990s, yes.
Q. Would these drugs have been used individually at that time, rather than in combination with Zidovudine?
A. Unfortunately that would be the case. Remember again, over time if there was one drug available, you worked on that drug and the big debate sometimes was: did you add a second drug to the first drug or do you just switch to the new drug? And we were still learning about resistance.

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

Indeed, when we did change, there was some benefit but again that was short-lived. It was almost trying to buy time until better drugs became available.
Q. Right. So by the early 1990s, a patient may have been treated with Zidovudine or one of those two drugs we

spoke about on a named-patient basis?

A. Yes.

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

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

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

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

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

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

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

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

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

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

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

Q. Is that the same as thrombocytopenia?

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

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

A. Yes.
Q. Yes.
A. In certain conditions. I still use it in some of my patients who get recurrent pneumonia with HIV. The basis for that is there is a defect in antibody production in the subset of HIV positive patients and they can benefit from the use of this modality to prevent bacterial infections.
Q. Is that still used now?
A. No.
Q. No.
A. It is used for the conditions I have listed here but not for HIV treatment per se. It would be used for other things.
Q. You tell us in the next paragraph about --
THE CHAIRMAN: Could I ask a question before you pass on?
Professor Leen, you mentioned a short time ago that you have experience of patients coming and asking for drug therapy using preparations that have not yet been proved to be effective, and sometimes you would give in if it weren't going to do harm and so on. Was this right across the range of your patients or were there particular pressure groups that seemed to be better informed than others about emerging therapies?
A. I think all of them.

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

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

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

A. True, yes.

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

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

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

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

A. There are quite a few of these.

THE CHAIRMAN: There are?

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

THE CHAIRMAN: Thank you very much.

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

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

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

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

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

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

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

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

But then again, it was easier to make the guidelines

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

developing knowledge?

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

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

A. And preventing it as well.

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

A. The treatment for PCP?

THE CHAIRMAN: For PCP.

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

THE CHAIRMAN: Yes.

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

THE CHAIRMAN: Professor James is suggesting to me that

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

A. I agree.

THE CHAIRMAN: And that happened just bit by bit.

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

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

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

THE CHAIRMAN: Yes, thank you very much.

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

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

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

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

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

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

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

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

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

Q. And which one is that?
A. That's Delavirdine. But we have patients on it still -- on a named patient still on that drug. That's the one between the Nevirapine, Efavirenz in 1997.
Q. Yes. So we see there that the first protease inhibitor was Saquinavir, followed by Ritonavir, and Saquinavir was first used in 1995 and Ritonavir in 1996. When these drugs were first used, were they used on their own or were they used in combination with what already existed?
A. It's a very good question. I think it was used in combination with whatever was available. A lot of those patients may have had those other drugs as monotherapy, single drug, before, but nonetheless we just added that in to make sure that we get as strong a regimen as possible to suppress HIV.
Q. Yes. So you started to see improvement --
A. Yes.
Q. -- in treatment when you used these drugs in combination with another one?
A. For those patients who are able to take three drugs together from the start, the benefit was better and lasted longer because if, let's say, you have had exposure to some of the previous drugs, it is likely that resistance has already occurred and they are not as

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

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

A. Yes.

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

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

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

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

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

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

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

this.

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

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

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

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

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

change at that time in treatment for HIV?
A. It was an amazing time, completely changed the face of HIV and AIDS completely.
Q. Yes.
A. I have had patients who, you know, were getting married because they thought they were going to die. They got married in hospital because they can't deal with going anywhere else, and it would be to survive and, you know, some of them have got children and grandchildren now. It's amazing what this drug did to the whole HIV/AIDS. It was amazing. Really remarkable.
Q. Yes. Then you go --
THE CHAIRMAN: Ms Patrick, be conscious of the time. I don't know whether the stenographer is happy to go on. I think if you stop now. The stenographer can't keep it up forever.
(11.15 am)
(Short break)
(11.38 am)
THE CHAIRMAN: Yes, Ms Patrick?
MS PATRICK: Just before the break, Professor Leen, we looked at page 8 of your statement and the five large randomised clinical trials. I was asking you whether it mentions combination antiretroviral therapy against nucleoside analogue monotherapy. I asked you if these

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

A. Indeed.

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

consequences of HIV. Was PML a consequence of HIV?

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

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

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

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

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

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

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

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

three years.

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

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

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

Q. It must be easier for the patient?

A. Very much easier.

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

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

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

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

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

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

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

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

A. Yes, it may well do.

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

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

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

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

A. Definitely.

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

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

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

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

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

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

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

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

THE CHAIRMAN: It was crucial.

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

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

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

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

A. Yes, exactly.

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

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

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

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

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

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

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

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

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

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

because you are hiding it.

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

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

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

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

A. Changing mood.

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

was taking.

Why did the treatment cause weird or frightening dreams?

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

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

Q. Would that interrupt sleep sometimes?

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

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

changes. Is that right?

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

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

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

Q. Do some patients receive surgery for that?

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

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

Q. Yes.

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

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

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

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

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

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

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

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

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

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

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

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

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

Q. Thank you.

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

inhibitors. What is that risk?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Then below that you talk about the effect of HIV on the Hepatitis C virus and tell us that evidence suggests that in an HIV positive individual, progression to cirrhosis is likely to occur more frequently and at a faster rate than in an immuno-competent individual. Is that the case even if the viral load is suppressed?

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

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

A. Who are co-infected --

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

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

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

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

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

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

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

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

A. Liver-wise.

Q. Liver-wise, to cirrhosis?

A. Yes.

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

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

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

A. Yes, it would be.

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

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

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

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

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

options become available.

Is that looking like some time soon?

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

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

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

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

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

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

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

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

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

a successful cure of Hepatitis C.

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

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

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

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

A. Unfortunately so; yes.

THE CHAIRMAN: Yes, Ms Patrick?

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

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

Q. Yes.

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

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

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

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

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

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

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

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

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

the professor?

Questions by MR DI ROLLO

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Q. That would be at the City Hospital?

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

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

Q. Right.

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

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

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

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

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

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

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

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

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

MR DI ROLLO: Indeed.

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

MR DI ROLLO: Of course.

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

A. But the clinician knew?

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

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

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

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

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

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

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

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

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

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

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

them as well.

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

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

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

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

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

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

that's fine.

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

Mr Anderson?

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

THE CHAIRMAN: You would want to be involved.

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

MR SHELDON: No, thank you, sir.

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

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

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

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

Does that answer your question?

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

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

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

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

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

terms of guidance for doing those tests.

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

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

Further questions by MS PATRICK

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

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

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

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

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

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

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

Q. It does. Thank you very much.

THE CHAIRMAN: Professor, thank you very much indeed. I think you, from your point of view, have been living through a very challenging and interesting era.

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

THE CHAIRMAN: Thank you very much. We will adjourn.

(1.00 pm)

(The short adjournment)

(2.00 pm)

PROFESSOR CHARLES FORBES (continued)

Questions by MR GARDINER

THE CHAIRMAN: Good afternoon, Professor Forbes.

A. Good afternoon.

THE CHAIRMAN: Mr Gardiner?

MR GARDINER: Yes. Thank you, sir.

Professor Forbes, good afternoon.

A. Good afternoon.

Q. You have previously appeared before the Inquiry in connection with the B2 topic and that was on 28 April and of course, today, I'm primarily asking you questions about the B5 topic. The Inquiry asked you for a statement about topic B5 and sent you a schedule which listed the matters which we were asking you to include in your statement and that is [PEN0120362].

Do you have that?

A. Yes, thank you.

Q. Thank you. So these are the questions which we were asking you to address and you kindly produced a statement, which is listed in our database at [PEN0120411]. Do you have a copy of that?

A. Yes, thank you.
Q. Okay. So we are going to have to work between these two documents as best we can.
Just to get some context here, Professor Forbes, could you tell us in 1983/1984 how many haemophilia patients you had under your care?
A. Approximately 250 with Haemophilia A and B. But in addition there were other more unusual conditions like von Willebrand's disease. So the numbers went up to 300 or 400.
Q. Thank you. Which other doctors did you have to help you to treat those patients in 1983 and 1984?
A. We had a small team of doctors, mostly people who were there in training and they included a Dr Gordon Lowe, who is now professor and now retired, and a cohort of more junior people, who are not named here.
Q. Yes. When you say that Professor Lowe, as he now is, was "in training", could you explain a little bit more what you mean by that?
A. Well, he came to the unit as a senior registrar, which was -- it's a grade that has now actually disappeared but it was the senior of the staff in training, towards the end of their training. So he would come for three or four years to be rounded off, as it were.
Q. I presume that at that stage a senior registrar would be

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

A. Oh, certainly.

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

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

Q. So is it training in haematology?

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

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

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

The next question is:

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

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

"I started to work with haemophiliacs in 1965 in the

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

Then the next paragraph:

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

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

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

Q. Thank you:

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

Then paragraph 3:

"I think at this time ..."

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

A. Yes, yes.

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

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

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

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

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

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

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

Q. Yes.

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

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

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

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

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

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

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

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

In your answer you say:

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

The next question is:

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

Your answer is paragraph 5 where you say:

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

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

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

Q. Focusing specifically on --

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

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

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

When you became aware.

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

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

Q. Yes.

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

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

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

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

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

Then the question is:

"And then AIDS was discussed."

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

A. Yes.

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

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

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

I think the next bit is important:

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

Then reading on:

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

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

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

of the page there is a question to you:

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

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

"Well, it was a concern.

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

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

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

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

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

Q. Yes.

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

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

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

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

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

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

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

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

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

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

A. Yes.

Q. Thank you.

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

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

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

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

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

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

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

A. Yes.

Q. Did you wait for the patient to raise that issue or is that something that you would raise yourself?
A. Well, we would always discuss what we were going to do because most of these were -- there was an element of choice for the patient and I think that we would always give them what we considered the best advice, which was the use of cryoprecipitate.
Q. Yes. Thank you. If we could move on to question 6, please, the question is:

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

And I think that should be:

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

Your answer at paragraph 6 is:

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

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

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

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

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

Q. Is it possible that that was in 1986, Professor Forbes, that that happened?
A. It could well have been. These things all took time and obviously, once someone has had the idea of heat treatment to get a safe product, it does take time and study and it could well be 1986.
Q. Yes. Thank you. I would like to ask you a few questions about immunological testing in Glasgow and you have kindly provided us with a separate statement about that, which is [PEN0121328].
A. Yes, thank you. I have it.
Q. Thank you. The Inquiry's questions are at [PEN0120771]. There should be a schedule attached to that, if we go to the next page, please.
A. Thank you.
Q. Yes.
A. I have it.
Q. Thank you. The schedule sets out the questions that we would like you to address. Question 1 talks about the enclosed BMJ article, published on 15 October 1983, and entitled "Immunological abnormalities in haemophilia: are they caused by American Factor VIII concentrate?" And this reported a study of cellular immunity in a group of 19 haemophilia patients.
We have posed certain questions about that study. I

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

A. Yes, thank you, I have it.

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

A. Yes.

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

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

And you cite several papers there. The next paragraph:

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

And:

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

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

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

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

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

I think that quite clearly ... did."

You say:

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

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

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

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

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

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

Q. Yes.

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

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

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

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

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

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

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

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

A. We didn't know what they meant.

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

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

A. Yes.

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

A. Yes, I have it.

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

I'll just read the next question as well:

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

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

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

Professor Forbes, who decided that samples should be collected?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

A. Thank you, I have it.

Q. We see the heading of this article is:

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

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

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

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

A. Yes, yes.

Q. And Karin Froebel?

A. She was a local immunologist in Glasgow.

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

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

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

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

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

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

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

A. Absolutely.

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

column, we see just at the top left:

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

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

A. Yes.

Q. Thank you.

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

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

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

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

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

MR GARDINER: Okay.
THE CHAIRMAN: As shown in table 1. Do you think that's everybody, Danish as well as ...? I don't think so.

There are two separate groups of paragraphs.

A. Yes, I understand that.
THE CHAIRMAN: I think, the Danish come, 22, and then comments about that and then "In Scotland ..." We have the following details.

So at the moment I'm not getting the arithmetic to work. I think it's as simple as that. If they are overlapping groups, then they seem to overlap in a rather strange way, and of course that raises the question about whether samples were being collected from the two different groups. I would like, if possible, to be able to get some reconciliation or some explanation.
A. Well, I suspect it may not be all the 19 that were tested originally. That's the only thing I can suggest at this time. I don't know if that helps at all.
THE CHAIRMAN: It may be that we just have groups that may overlap. I think we may be back to Ms Dunlop's Venn diagrams with a small overlapping section in the middle somewhere. Clearly neither group represents the whole constituency that you had available.
A. Absolutely not.
THE CHAIRMAN: Yes.

A. Can't.
MR GARDINER: Sir, we are trying to find the section where it mentions the 40 per cent.
THE CHAIRMAN: 40 per cent is in the first page.
40 per cent is the -- I'm losing my hard copy references -- is on page 1445 of the Lancet article of 22 December, 1984. It's immediately above the discussion.
MR GARDINER: I think it's 40 per cent of the patients that had received commercial concentrates, as opposed to 40 of all of them.
THE CHAIRMAN: So it's the bottom section of the table, is it, that's referred to in that paragraph? Which doesn't work for me since it's two people representing 40 per cent of 25: I'm not sure that's right.
MR GARDINER: It's the patients that have received commercial concentrate, whether Scottish or Danish and it's 40 per cent of that group, sir; I think.
THE CHAIRMAN: Two out of 25? Two out of 25, if that's what the 40 per cent refers to. So there is a problem.
PROFESSOR JAMES: I have this now. So in this section called "healthy haemophiliacs" there is first a paragraph referring to the 22 Danish haemophiliacs. There is, second, a paragraph starting:
"In Scotland ..."

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

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

PROFESSOR JAMES: The important thing is that the sentence:

"40 per cent of subjects receiving commercial factor concentrate either alone or in combination with local products ..."

Refers to both Denmark and Scotland put together.

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

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

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

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

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

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

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

Then question 10:

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

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

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

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

Dr Melbye carried out the testing on these samples?
A. I think that the answer would be probably not at that time. It's difficult to remember but this was very much a moving situation and the whole question of consent at that time was very woolly. Certainly later on it tightened up immensely and has changed even more since then. So I don't think that we would be asking for consent for storing samples but they might be told that they were being stored. So I'm very unclear as to when all these things happened.
Q. Yes. How would it have worked? How would the samples have got to Dr Melbye?
A. He actually came to Glasgow to pick them up and they were passed over to him in a frozen state.
Q. Yes. Who passed them over to him?
A. I'm sure it would be me.
Q. Yes. You said that patients were probably not asked for their permission to have them tested by Dr Melbye?
A. I think that is the situation. I don't think that at that time there was any concern about consent because we assumed that people would want to know about what was happening and what the implications of this new test would be. So I don't think that we asked for consent.
Q. Yes. Do you have any doubt about that, Professor Forbes?

A. I'm quite sure that we didn't ask at that time.
Q. Thank you. If we just read on in that paragraph, paragraph 9, you say:

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

And so on. Could you explain to us what obtaining specific consent involved?
A. I think the important thing is that you are telling patients what is going to happen and why it's to happen and to ask their consent for it to happen. This was very much a change in the ethos of medicine. Until then the implication was that if you went to a doctor with a problem, he would do his best to find the cause of it, without asking your consent for blood samples or whatever, and that was how things were at that time.

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

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

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

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

Q. Yes. Thank you.

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

A. Yes, indeed.

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

A. And a very effective lady she was too.

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

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

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

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

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

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

A. Yes, I see it.

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

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

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

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

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

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

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

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

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

Q. Yes. Thank you.

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

THE CHAIRMAN: Is that a suitable time?

MR GARDINER: Yes, sir.

THE CHAIRMAN: We will have a short break.

(3.10 pm)

(Short break)

(3.30 pm)

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

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

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

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

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

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

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

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

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

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

The questions are:

"Were the 77 patients different?"

We have looked at that:

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

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

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

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

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

Then 2.3:

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

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

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

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

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

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

Q. Has the department's policy changed?

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

Q. Yes, thank you. Thank you.

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

A. Yes.

Q. The question was:

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

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

"What arrangements were made for patients to be told

of positive test results?"

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

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

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

A. Yes.

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

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

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

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

A. Well, usually myself.

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

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

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

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

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

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

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

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

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

Dr Follett?

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

Q. Yes.

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

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

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

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

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

Q. Thank you.

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

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

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

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

Q. That's December 1984.

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

Q. Yes.

A. So ...

Q. Could we have --

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

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

A. Yes, indeed, which I was there.

Q. And you were there. If you look at paragraph 4:

"Dr Forbes described the findings relating to HTLV-III antibody seroconversion in a comparative study of haemophilia patients in Glasgow and Denmark. This study would shortly be published in the Lancet."

So you must have had the results by that stage?

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

Q. Well, the meeting is dated 29 November 1984.
A. So it must have been before that.
Q. Yes.
THE CHAIRMAN: What would have happened in between? From the point at which the paper was submitted, it would be reviewed by the editors and a decision sent back that it was available for publication or was to be published?
A. Yes.
THE CHAIRMAN: So that by November then, you knew that it was to appear in the Lancet.
A. Yes.
THE CHAIRMAN: So it had been accepted for publication?
A. Yes.
THE CHAIRMAN: How long would normally elapse between submission and that information, Professor Forbes?
A. It depends on the journal but it could be three months easily.
THE CHAIRMAN: And before that, because you have Dr Melbye involved, you will be sending drafts back and forward?
A. Absolutely.
MR GARDINER: I'm just trying to work out some dates here, Professor Forbes. Our information is that at this period the only tests for the virus were experimental ones. Dr Melbye was able to do testing. Dr Tedder was able to do testing. And it wasn't really until at least

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

A. Yes.

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

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

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

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

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

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

Q. Yes.

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

Q. Yes.

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

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

"Dr Gibson reported the anxiety felt by parents of haemophiliac children treated at RHSC Glasgow, [Yorkhill], where imported Factor VIII had been used

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

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

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

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

A. Sorry, I don't know.

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

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

I think we were really quite successful."

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

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

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

A. Yes.

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

A. No, but I was clearly there.

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

A. Yes.

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

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

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

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

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

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

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

Q. Why did you think that? What was your reason for coming to that view?

A. Well, no matter what, the bad news was going to be there at some time. We didn't understand fully what the implications were but we suspected from what we knew already about the natural history of the disease that these patients were being given almost a death sentence, because most of them in fact up until that time, the ones who were diagnosed with positive antibodies, died, and died quite quickly thereafter, within the year. So we felt that it was only fair to them and their families to know what it was all about. But, as I say, it was a very divided view.

Q. Did the communication of the results have any implications for the treatment that you could offer the patients?

A. Well, there was virtually no treatment at all at that time and you have heard of the successful introduction of different drugs over the years but what we heard today was mainly 10/15 years further down the line, when drugs became available. When we started out, there was virtually nothing that was going to be effective.

Q. Yes. Just looking at the next question, did your

practice about informing patients of positive test results change between 1984 and 1987?

A. I don't think it changed between these dates. We had a very open policy and tried our best to be as up front as possible. So it didn't change. It was always there.

Q. Was there a point where pre-test counselling was introduced?

A. I think that would be the norm nowadays, that to get consent you have to tell them what you are going to do and why you are doing it and what the implications are. So I think pre-test counselling is very much a more recent addition.

Q. Yes. Where would that date from, would you think?

A. I think it would be well into the end of the 1980s/the beginning of the 1990s.

Q. Yes.

A. By that time we had a better idea of what might be done for the patients and what drugs would be available and what effect they would have, and also about the spread of disease, particularly to other family members and so on. So it's a different situation.

Q. Yes. Thank you.

Just moving on to the next topic, which is going to be one of our last, this is all to do with a meeting of haemophilia patients in Edinburgh, and we have it as

19 December 1984. If we look first at the questions, questions 16, right through to the end, are all about what happened at the meeting, what happened before the meeting and so on. I think you answer them in your paragraphs 14 to 19. Just looking at paragraph 14, the question you are addressing here, first of all, is: what was the purpose of the meeting on 19 December 1984? You say:

"I think some of these questions probably should be asked of Dr Ludlam, who organised the meeting in Edinburgh on 19 December 1984. It was to inform a group of patients from Edinburgh about what was happening with the virus and the implications thereof. I really don't know why I was invited to go but I was, and invited to chair the meeting."

Just pausing there, Professor Forbes, are you able to say now why you were invited to go?

A. Well, we have had a lot of discussion about my failing memory and clearly I went with a view to chairing the meeting and to do that happily. I had thought in retrospect that it was only Edinburgh patients but my colleagues tell me that in fact it was a general invitation to patients to come to the meeting, which was in Edinburgh, and organised by Dr Ludlam.

So I am afraid that I have a major blank in some

parts of this but I do remember the meeting and I remember the people who were there, and it was Chris Ludlam who was the speaker for Edinburgh and Brian McClelland from blood transfusion, and there was a social worker as well, who I think you are going to hear tomorrow. So I have a blank about parts of it but I do remember some of it and it was a general discussion to try and educate the patients and their families, who came along, about what might or might not be done and what was available by way of treatment and what was available to help them cope with all the different problems that are now arising.

So it was very much an educational-type meeting, held in Edinburgh.

Q. Yes. Well, I would like to you be careful, Professor Forbes, to tell us what you can remember and not what you may -- how shall I put it?

A. Have learnt.

Q. Have learnt. If you can try to be careful about that. Do you remember what discussions you had before the meeting?

A. I don't think we had any discussions from my defective memory. I don't think -- there was no agenda set and there was nothing that we were told not to say or to say. So it was just an open meeting.

Q. Yes. How many people do you think attended?
A. Well, I remember the lecture theatre being pretty full and I have no idea how many people but I'm since told that it holds up to 200 but I don't think there were 200 people there. But less than that. But it was pretty full.
Q. You have put 20 people there, so that sounds more. What you are telling us now is more than 20?
A. Yes, I'm being persuaded. So I have to be careful what I'm saying. I thought from memory it was about 20 people but there we are.
Q. If we can try to stick to your memory, Professor Forbes.
A. Yes, sorry.
Q. And your memory, is it still telling you 20 people?
A. Well, I just remember the few people in front that certainly asked questions, and I didn't think it was as many as I'm now being informed about. So 20 people may be wrong.
Q. Yes. Do you remember who spoke first?
A. Yes, Chris Ludlam.
Q. And can you remember broadly what he told the meeting?
A. I have no recollection of anything he spoke about, but it was all relevant to the background information on this new virus.
Q. Yes. Was it more specific than a new virus, can you

remember?

A. I don't remember anything that was more specific but -- you must remember that many of the people in the audience had already read about this from the media and newspapers and so on. So I'm not sure that he was telling them anything particularly new.

Q. You say here at paragraph 17 that you think the meeting went on for about two hours?

A. I think about two hours. I remember quite clearly going home on the train after it and it was dark. So it would be about two hours, I would have thought.

Q. When do you think it started?

A. About 7 o'clock. It was in the evening.

Q. Paragraph 18. You say:

"I see from the note that Dr McClelland (who was from BTS) was there but I don't remember what any of them said."

When you say "the note", what note are you referring to there?

A. I think that was something that you had sent. One of the questions maybe that you had asked.

Q. Yes.

THE CHAIRMAN: 21.

MR GARDINER: Yes, question 21, thank you. You say:

"From memory I believed that patients had been told

about the tests that were done but I don't remember if any of the people at the meeting had not been tested and subsequently wanted to be tested. Most of the patients seemed to know what kind of treatment they had been on and I don't remember that as a particular point of discussion."

You seem to be describing something a bit more specific than just a general concern about a new virus?

A. Oh -- and how they might have been exposed to the virus. That would be the question of treatment.

Q. Yes. Do you remember what the people that came were told about the possibility of having been exposed to the virus?

A. I think they were told that some of them had been exposed but there was no particular test available at that time, but that was coming on stream and that in the course of time they would in fact have communication, if they wished it, from their haemophilia director. So it was very early days.

Q. So communication, if they wished it from their haemophilia director. Do you have a recollection, as you are sitting there, Professor Forbes, of those words being said at the meeting?

A. I have no recollection of any words that were said at the meeting but that would be the implication, that they

would be told in the course of time if there were any further tests, or if they wanted further information, they could come and ask about it. But I have to say that my memory is very hazy about this although I certainly do remember going home from the meeting.

Q. Yes. But you are telling us that you have a memory of that message being imparted, that --

A. That, I think, is right. I don't remember what words were said.

Q. Thank you. Then just reading on, paragraph 19:

"The patients were quite generally well-informed. They were not particularly told that HTLV-III could be a terminal illness although many of them knew of patients who had died, particularly in America. As far as I know, there was no discussion about Scottish blood products as opposed to American blood products. In particular I can remember the mood of the meeting and I certainly don't remember any hostility from the audience."

You have a personal recollection of that, Professor Forbes, do you?

A. I have a memory that there was no hostility shown at all and one would have thought that there might have been but I'm not aware of it.

Q. You say:

"I think they were generally shell-shocked at the information that had been given to them."

How did you come to form that view?

A. Well, the audience became very quiet at some points and that would be an implication that they were digesting what they had been told about what was happening, but I have no recollection of any hostility towards anyone at all.

Q. Yes. (Pause).

Professor Forbes, can you remember if anybody else spoke to the meeting apart from Dr Ludlam?

A. I know that Dr McClelland was scheduled to speak and I'm sure he did but I don't remember the detail of what he said, but I don't remember anyone else speaking. But there was a general question and answer session so no doubt others did speak.

Q. Yes. These were questions from --

A. From the audience.

Q. Can you remember what sort of questions were being asked?

A. I don't remember any specific questions but they were very general information-seeking questions.

Q. Yes. Thank you.

Sir, I propose to leave that now unless ...

THE CHAIRMAN: I'm still in some state of confusion over the

timing of the Melbye exercise.

You gave me earlier an indication, professor, of the sort of timing that could be involved when an article was submitted and reviewed and eventually published; which if it had applied in this case would have thrown one back several months into 1984.

If we look at the internal information, it might suggest that in this case the process was very much faster. So would you like to look at it with me, please, and see why I'm saying that?

A. I should just add that the Lancet often had a more rapid publication schedule than other journals. They may actually give dates on that paper, when it was first submitted.

THE CHAIRMAN: It doesn't. I have looked for that.

A. Okay.

THE CHAIRMAN: But there are two bits of information in it that may bear on this particular point.

I think we have it anyway. Can we look at the second page, please. [LIT0011702].

If you look at the top of the left-hand column it states in the first place that blood was taken in Glasgow between December 1983 and July 1984.

So July 1984 is clearly in the frame. But if we look at the end of the paragraph headed "Results", we see that

it's narrated that a Scottish patient died in late October 1984. Have you found that?

A. Yes, yes.

THE CHAIRMAN: Do these dates help at all in giving a reference point for the Melbye study?

A. No, I think with regard to the second point, you say the death of a patient, I think that would be added in the text and probably is not relevant particularly to the actual study and the samples and so on. But it helps to date it from some point. So at least that was in the text that went to the editor of the Lancet.

THE CHAIRMAN: But the study itself could have been somewhere after July.

A. Yes.

THE CHAIRMAN: And possibly soon after July.

A. Yes.

THE CHAIRMAN: Possibly in July? That's one point in the article. The other is the impact that the information about the tests may have had on you because, one way or another, by this date, and therefore before the December 1984 meeting, it was known that a Scottish Haemophilia A patient had died of AIDS. Was that not a factor that might have caused you to be somewhat disconcerted?

A. Well, any death is disconcerting and certainly that does

put a date. But, of course, the samples from that patient may have been tested and tested some months before for the study.

THE CHAIRMAN: We know it was May and July, at least the samples are measured as at May and July of 1984, just above the death.

A. Yes.

THE CHAIRMAN: So he was being studied in the same period, but it doesn't help you beyond that?

A. No, I don't think so.

THE CHAIRMAN: Thank you.

MR GARDINER: I just have one article I would like the professor to look at, sir.

Could we have [LIT0010829]? You don't have a hard copy of this, professor.

A. No.

Q. If you could see that, it's an article from the Scottish Medical Journal, "Acquired Immune Deficiency Syndrome -- an overview."

You will see volume 30, January 1985, number 1. If we could go to 0834, we see in the middle of the page there that this is an article that you have written, together with JA Gracie, Karin Froebel, R Madhok, Professor Lowe. Does it ring any bells with you, Professor Forbes?

A. Oh, yes, I remember writing it.
Q. Yes, thank you. Could we have a look at page 5, which is 0833? The left-hand column, about two thirds of the way down, the sentence that starts "The one haemophiliac ..." which is a bit further up, actually. That's it, thank you. So just reading there:

"The one haemophiliac who has died of AIDS in Scotland received a large amount of commercial Factor VIII from the USA whilst being treated in England. The implications are that in Scotland the AIDS virus does not seem to have affected the donor pool as yet but a test for HTLV-III virus antigen, which should be available soon, will be valuable in screening for virus contamination."

Professor Forbes, this is an article which appears in 1985 and it must have been available for revision quite close to the publication date, and we are wondering how that statement has come to be made in this article, given what we have heard about patients being infected earlier than this.
A. I'm not quite sure that I understand the point you are making. Could you go back over it?
Q. Well, the statement is:

"The implications are that in Scotland the AIDS virus does not seem to have affected the donor pool as

yet but a test for HTLV-III virus antigen, which should be available soon, will be valuable in screening ..."

We know that by this stage the AIDS virus has affected the donor pool in Scotland.

A. Well, I think my understanding from this is that we thought that the contaminated batch of Factor VIII had been given when he was in England.

Q. I'm thinking of the implicated batch which was responsible for infecting the Edinburgh cohort?

A. Oh.

Q. Of course that was what the meeting in December 1984 was about.

A. But there was no doubt that it was inevitable that the donor pool in the United Kingdom was going to be affected as the disease was brought into the UK, and that people who were HTLV positive were going to be giving blood at some stage. So that's almost a logical sequelae of what we thought would happen.

THE CHAIRMAN: Professor, were you the editor of this journal at some stage?

A. Yes.

THE CHAIRMAN: At this time?

A. Yes.

MR GARDINER: So, Professor Forbes, if you remember, I showed you the minutes of the meeting

from November 1984.

A. Yes.

Q. Perhaps we can have them up again. [SNF0010255]. Can we have a look at paragraph 3? Can you see that?

A. Yes.

Q. "Dr Ludlam explained the circumstances in which it had been discovered that 16 haemophilia patients treated exclusively with SNBTS Factor VIII had developed antibodies to HTLV-III, leading to the presumption that a Scottish plasma pool had been contaminated by a donor carrying HTLV-III. Various aspects of the epidemiological, pathological and ethical problems were discussed."

So that seems to be Dr Ludlam reporting that the AIDS virus has affected the Scottish blood donor pool, does it not?

A. Yes, indeed.

Q. So that's the purpose of our question about this article. We were wondering how that statement had found its way in.

A. Well, I'm not sure when the article was written but it would certainly be before the date of the publication, probably a month before. So when I wrote it, I don't think I had either been at this meeting or this had not impinged on my conscious level.

Q. Yes.
A. So it certainly was the beginning of the anxiety about contamination of the donor pool.
Q. Yes. Well, Professor Forbes, just for completeness, as we lawyers say, if we go up to the top of that page, we see, just to remind you, you were at that meeting.
A. I admit that fully.
Q. Sir, I don't have any more questions for Professor Forbes?
THE CHAIRMAN: Thank you.
MR GARDINER: Thank you very much, Professor Forbes.
THE CHAIRMAN: Mr Di Rollo?

Questions by MR DI ROLLO

MR DI ROLLO: Yes, sir, thank you.
Can I ask you about the December 1984 meeting first of all? One of the things that you have indicated in your evidence today is that you have obviously discussed this before coming to give evidence today with colleagues. Is that right?
A. Yes.
Q. Who have you discussed it with?
A. Mainly with Gordon Lowe.
Q. And who else?
A. With Chris Ludlam.
Q. Right.

A. Who was there. And I think these are the only two people I have actually met up with.
Q. When did you discuss it with Dr Ludlam?
A. It was after the last time I was here, which is maybe a month ago.
Q. Right.
A. Because I was surprised at what I had heard about the meeting, that it was in fact a meeting, and indeed my colleagues in Glasgow said that it was a meeting for the whole of Scotland. But I had thought it was only a meeting for the Edinburgh patients.
Q. How long did you discuss it for with Dr Ludlam?
A. How long?
Q. Yes. How long did you have a discussion about this meeting?
A. I think we were talking over lunch.
Q. Did Dr Ludlam indicate what his recollection of matters was in the course of that discussion?
A. He was clearly of the impression that it was a meeting which was attended by Glasgow as well as other haemophiliacs round the country. And he also said that I must have remembered that or should have remembered that, but I certainly didn't.
Q. Do you remember that? You didn't remember it when you had your discussion with Dr Ludlam. Do you remember

that now?
A. No, I still don't remember it now but Dr Lowe had said that we had in fact written, as a result of the meeting, to various patients in the West of Scotland and that I had written the letter to them. So it may be true. It's just defective memory, I'm sorry.
Q. Let's just have a look at that. Did you have a discussion with Professor Lowe after you discussed it with Dr Ludlam, this meeting? In other words having spoken to Dr Ludlam --
A. I think he was at lunch with us. I think we were all discussing it together. They were amazed that I had not remembered so much of what went on.
Q. Professor Lowe wasn't at the meeting at Edinburgh in 1984.
A. I think that would be before his time.
Q. Right. And whether or not you wrote to patients after the meeting isn't really relevant to the actual meeting itself and who was at the meeting. Is that not fair?
A. I think that we were reporting back to the generality of patients.
Q. Right.
A. That's my understanding of what I'm told.
Q. Have you ever seen a letter to that effect?
A. No. There must have been a letter and it must have gone

out.

Q. Can we just concentrate then on your recollection of the meeting at Edinburgh, because we are not really going to get very far if we think about what other people's recollections are?

A. Okay.

Q. Your statement to the Inquiry, which we have seen, and your original recollection, it doesn't appear that there was anybody from Glasgow, ie, Glasgow patients, at that meeting in Edinburgh. Is that correct?

A. Well, that was my recollection.

Q. Yes. That there were no Glasgow patients?

A. That's what I think.

Q. Right. In your statement you say there were about 20 people or so at the meeting other than the doctors that were present. Is that correct?

A. Well, that's what I thought and shows how defective memory can be.

Q. Your memory may be perfectly accurate. Why is it defective?

A. I would have said my memory is not wonderful nowadays. But that is what I said and that's what I thought at the time.

Q. All right. Are you saying that you don't actually now have any understanding of why the meeting was held?

A. My understanding was it was an educational exercise for patients in Edinburgh.
Q. Do you recall whether it had any link to what we saw there in the document that was put before you about what Dr Ludlam had discovered in relation to his patients?
A. I have no recollection of that at all and that certainly didn't come out at the meeting, as I remember.
Q. Do you know why you were invited to go to the meeting?
A. I have no idea but I had known Dr Ludlam for a long time and it seemed reasonable to have a neutral person at it, as I saw.
Q. In the minutes of the meeting we just saw, we noticed there that there is mention of discussion of ethical problems. This is the November meeting that we saw just now that you said you were at. What were the ethical problems in relation to what had occurred? Do you know?
A. I don't think it was anything to do with the meeting that was held in Edinburgh. I'm not aware of any ethical problems arising from that.
Q. I'm referring, I think, to the ethical problems that might arise as a result of the fact that patients had been tested without their knowledge and the tests had been proved to be positive, and whether any ethical problems would arise as a result of that.
A. Well, I don't think in these days that there was any

ethical dilemma at that time, and it certainly wasn't perceived by the people involved at that time.

Q. You say that, Dr Forbes, but Patricia Wilkie told us yesterday that you had originally carried out tests on a non-named-patient basis and that when one or two of them had proved to be positive, you decided to stop and you were concerned about that and she said that you stopped testing for ethical reasons. Now is she wrong about that?

A. Well, I don't remember that happening but certainly we were appalled when we found that some of our patients were HTLV-III positive. That was a devastating time in one's life, that this virus had crept in to our patients.

Q. When you sent samples for testing originally, did you do so on a named or on an anonymous basis?

A. The samples were all labelled. So they were not anonymous. They were, therefore -- I think, it is important to say that there was action required to be taken when they were found to be positive.

Q. Right.

A. And we could identify the people who were involved, and we told them.

Q. Right. So as soon as you discovered the outcome of these tests, you took steps immediately to inform them

all of the results?

A. Yes, all of them.

Q. Why did you do that?

A. On a personal basis. Well, I think it was important. We were going to tell them very bad news. There were implications not just for them but for their families and their lifestyle, and it was to my mind very important that we tell them what had happened. Nothing was being hidden away.

Q. Did you understand that, in December 1984, a similar thing had occurred at Edinburgh, in that tests had been carried out and that specific individuals were identified or known to be HTLV-III positive, and that was the purpose of the meeting or one of the purposes of the meeting in December, to tell the patients of that fact? Was that what you understood was going to happen?

A. I don't think I knew that at the time.

Q. I see.

A. But I think it was about that time that in fact the patients were told what had happened.

Q. Was it your view that patients should have been told then the outcome of any tests that had been carried out on them?

A. Well, I think they were very soon after or as soon as possible thereafter.

Q. That's what your patients were told?
A. Yes.
Q. Were your patients told before the article was published in the Lancet?
A. I can't remember the chronology. We had a policy of writing to them when they had a positive test and inviting them to come in for a discussion and that was when they were told.
Q. So I think the question was whether or not you would have told your patients before the article was published. Are you able to help on that?
A. We would start to do the process of telling the people, and that takes many weeks. So whether the article was published or not, I can't say now, but the process of telling them had started.
Q. Sir, I don't think there are any other questions that are going to elicit any useful evidence.
THE CHAIRMAN: Yes. Mr Di Rollo asked you a question. I don't think you answered directly, professor. It was: was it your view that patients should have been told the outcome of any tests that had been carried out on them and your answer was, "Well, we did tell them," but I think that the question was directed towards what motivated the telling rather than the telling. Did you think that they ought to be told?

A. Well, I'm not sure that I really understand the subtly of your point.

THE CHAIRMAN: Well, it's the difference between just doing something casually and doing something as in implement of an obligation that you felt.

A. We did feel an obligation and the positivity was devastating to us but also to the patients and to -- we felt an obligation to tell them as best possible what the implications of the test for their routine lives and their way of life and for their families and so on. So we did feel an obligation, and as rapidly as possible that was done.

THE CHAIRMAN: Was Dr Wilkie involved in that?

A. Eventually. I'm not sure just exactly when she came into post but she was certainly involved latterly, very deeply involved, in telling patients in association with all the other helpers who were there.

THE CHAIRMAN: "Headhunting" is a particular expression in current parlance. Had you really sought her out to get her help for this purpose?

A. Well, it was fortuitous because she was already working with us on something which she was very expert in, which was the genetic counselling of various things, of which part of it was genetic counselling of haemophilia. But her employer at that time was to do with adult

polycystic kidney disease. And she was there in post and agreed to do the other part of the job, which I think became much more important to her and to us.

THE CHAIRMAN: Mr Anderson? Mr Sheldon?

I have only one further matter to ask you to look at and that is a quotation on page 3 of [LIT0011702]. I imagine it just comes fortuitously at the end of the article that we have been looking at. Have you read it?

"'Viewing medicine as a battle too often reduces the patient to an object -- a fragile boat, a rudderless frigate, a hapless barge of statistical misfortune tossed upon the stormy seas of illness. A doctor, in turn, views his responsibilities as a naval skirmish -- a confrontation to be prepared for, fought, and won. The patient in this perspective is entirely passive. He hopes only to be saved. The doctor sends in his armada and tries to occupy disease's strategic islands; or occasionally he has to retreat. What he does not do is relate well to his patient. The family of the patient is also relegated to the role of helpless bystander ... with distressing regularity, families are excluded from any substantive involvement with the physician ... they hover compliantly in the background while physicians, medicine's gladiators, unsheathe their swords and do battle with disease. What a waste of powerful, and

potentially healing, resources!'"

The language might not be yours but is that a proper characterisation of the paternalistic attitude of the period?

A. I think it's a splendid quotation.

THE CHAIRMAN: Thank you.

We will adjourn.

(4.40 pm)

(The Inquiry adjourned until 9.30 am the following day)

I N D E X