

Thursday, 13 October 2011

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(9.30 am)

THE CHAIRMAN: Good morning. Ms Dunlop, gentlemen, thank you very much for the help you gave me yesterday in considering the steps that might be taken from now on.

As I said yesterday, really very little is carved in letters of stone in an Inquiry like this but I think that it would be helpful to everybody if I were to set out now what I see as the way forward and what I would envisage being the framework, subject to any applications that are made hereafter.

In saying "subject to applications", I should make it clear that I think from now on, informality is simply not acceptable. I have tried to make the point before. But if anyone wants to deviate from the anticipated course of events, I think it would be necessary now to have a formal written application, supported, as is appropriate, intimated to everyone else, so that everyone can see and consider just exactly what the implications might be of change. But for the time being, what I envisage happening is this.

Each participant will produce, by the end of January 2012, a statement of the issues thought to arise on the evidence and to require a decision by me in writing the final report. I don't want a story of

1 absolutely everything; it's to focus on the issues that
2 it's thought I will have to decide.

3 I would like those issues to be arranged by
4 reference to the topics that have been used in
5 marshalling the oral evidence led in the Inquiry, both
6 to date and between now and the closing stages of the
7 oral evidence.

8 I wish to emphasise that each issue should be
9 supported, as it were, by a general reference to the
10 evidence that's considered to be relevant to the
11 resolution of the issue.

12 What I have in mind is, for example, that one would
13 say, "Dr Cash, Day 48, between pages 1 and 20". I don't
14 want a detailed analysis, but, because I have done
15 a certain amount of analysis of the evidence myself, if
16 I have a reference to the broad areas, then it will
17 enable me to find out pretty quickly whether we are
18 talking about the same body of evidence or something
19 different. So I would like that to be part of the
20 application.

21 I will make it clear that it will be acceptable for
22 the statement to be produced in parts by the individual
23 counsel who have taken the lead in the examination of
24 specific issues. I think that applies primarily to
25 Inquiry counsel and to Mr Di Rollo, but I'm not going to

1 require things to be cobbled together; indeed, I would
2 prefer to have the identification of the person who is
3 making the contribution quite clear because it will help
4 me in responding to it.

5 The evidence for the purpose -- and this is a point,
6 I think, raised by Mr Di Rollo yesterday -- may include
7 statements of witnesses obtained by the Inquiry team,
8 whether or not the particular witness has been called to
9 give oral evidence. I think everyone knows that relates
10 to the very large volume of material which will instruct
11 the general impressions, for example of the adverse
12 consequences for patients of suffering from one or other
13 of the conditions that are the subject of investigation.

14 But I should make it clear, as certainly counsel
15 will appreciate but others may not, that evidence that
16 has not been open to be tested may be inherently less
17 satisfactory than evidence that has been led orally and
18 where the witness has been available to be examined by
19 others. Also, it will be understood that what I have in
20 mind are the signed statements of witnesses, because the
21 signed statements again are likely to be inherently more
22 acceptable than drafts or documents that have not been
23 signed by the party.

24 Also, I will not entertain submissions or arguments
25 that relate to issues that could have been explored with

1 witnesses who were called and which were not, for
2 whatever reason.

3 As parties will appreciate, I have heard of or
4 I have seen, comments in other quarters directed against
5 particular people who have been led as witnesses here.
6 I simply will not accept, as part of this process, an
7 attempt to introduce allegations that have not been
8 properly explored before the Inquiry, and I'm likely to
9 be extremely critical of anyone who tries to introduce
10 such a matter.

11 Thirdly, I will not entertain fresh evidence at this
12 stage at all.

13 Because of that last stricture in particular, I'll
14 turn to my next chapter. It will be open to any
15 participant -- and for this purpose I include Inquiry
16 counsel -- to launch a statement of representations that
17 any particular issue identified in the statements that
18 have been lodged should not be the subject of further
19 discussion or examination. I really want people to
20 ensure that at the end of the process we know what ought
21 to go forward for detailed discussion and what should
22 not, and there may well, for all I know, be issues that
23 any participant at all seeks to introduce at this stage
24 that, taking a broad view, really should not be taking
25 up the Inquiry's time, and I would like these matters to

1 be cleared out before one goes any further.

2 Each representation of that kind will have to be
3 accompanied by an application for a hearing and an
4 estimate of the time required for disposal of the
5 matter, and that application must be intimated to all
6 other parties so that they have an opportunity to take
7 part in any debate that arises out of the point.

8 I have no idea what might arise but it's clear that
9 there could be issues introduced, or perhaps even the
10 way they are expressed, that provokes an adverse
11 reaction from other participants and there could be
12 a benefit and a bit of discussion before finalising the
13 point to take it forward.

14 The period for any such representations will expire
15 on 11 February 2012. That, of course, is on the
16 assumption that the 31 January date is adhered to
17 strictly.

18 Having regard to the general restriction on the
19 introduction of new evidence at this stage, I intend to
20 invite parties now to consider whether they wish to make
21 any applications for the introduction of new evidence in
22 the Inquiry.

23 Any such application must be made within four weeks
24 of today's date in relation to business that has already
25 been dealt with. I can't put an application limit on

1 evidence that we have yet to hear altogether. That
2 would not be appropriate, but if it relates to material
3 that has already been led, I wish the application within
4 four weeks. And that, Mr Di Rollo, you can take it,
5 relates in particular to Tamburrini because that's the
6 only case I know where this may arise, but if there are
7 others, the same stricture will apply.

8 The application must identify the issue that arises
9 and the existing evidence on the matter with the same
10 degree of particularity as I have already mentioned, and
11 it should indicate why it is thought that the evidence
12 that has been heard to date is not sufficient to dispose
13 of the point.

14 As I say, I have in mind the particular case of
15 Tamburrini and yesterday I made some comments about the
16 broader issues involved in introducing evidence of that
17 kind. That's all I propose to say on it. It's entirely
18 a matter for the participants to decide whether they
19 should make such an application or not. I would only
20 hope that if any such application is made,
21 Mrs Tamburrini and the others involved are fully and
22 properly advised of the potential for adverse
23 implications that can arise from their being led in
24 evidence on a matter of this kind. That's just
25 a reflection of past experience. People can be very

1 badly hurt by what happens at a hearing of this kind and
2 the risk should be fully understood before any such
3 application is made.

4 Going on to the next stage, before 31 March 2012
5 each participant will produce a statement of answers to
6 the questions that have been posed in the statements of
7 issues, revised by any representations, et cetera, that
8 have been made and disposed of in the interval.

9 The particular statements must provide the
10 participants' answers to their own questions. It's not
11 just an attack on other people's work. I want to know
12 what those who have posed a question propose the answer
13 to that question ought to be.

14 Apart from that, I'm not requiring any other
15 participant to answer all of the questions that others
16 raise. It will be open to each individual participant
17 to deal with such issues as they think require to be
18 dealt with by me in arriving at final views.

19 I think that's as far as I need to go on that. I'm
20 not trying to put handcuffs on people at this stage.
21 I don't want work to be done that's not necessary and
22 I hope that that is sufficient basis for parties to
23 exercise a degree of common sense in how they approach
24 this issue.

25 In the light of the written statements, the

1 representations and all the other procedure that may
2 well have taken place by this stage, I think it remains
3 an open question whether there will be any need for
4 a further hearing for oral submissions or not. I don't
5 want to foreclose that and I don't want to attempt to
6 determine in advance what the scope of any such oral
7 hearing should be. But I think that what I ought to do
8 is to give an indication of the mechanism that I think
9 would be appropriate for dealing with such matters.

10 So it will be open to any participant within two
11 weeks after 31 March 2012 to make a written application
12 for an oral hearing for the purpose of making a closing
13 statement on any issue arising on the evidence that has
14 been specified in the statements of issues, et cetera,
15 lodged prior to 31 March 2012.

16 I'm not going on entertain an application to deal
17 with something totally new. It's to deal with matters
18 that have been properly focused already. I would expect
19 the statement to specify again, in general terms, the
20 evidence relied upon in suggesting that an oral hearing
21 is necessary and I would like a clear statement of the
22 purpose that is thought to be promoted by hearing oral
23 submissions at that stage.

24 I want to make it absolutely clear that at the
25 moment at least, I have no intention of allowing new

1 evidence at this stage. Indeed, I would be inclined to
2 resist it and the only reason I don't make an absolute
3 prohibition is that I think in this, as in other
4 matters, one must appreciate that things can happen that
5 may lead to proposals for further procedure and it would
6 be inappropriate to exclude the possibility. I can't,
7 in other words, achieve a mathematical certainty in
8 defining a role that would prevent anything else
9 happening. The possibility of other factors just can't
10 be excluded.

11 But apart from that, Ms Dunlop and gentlemen, that
12 is an outline of where I think I have reached in the
13 light of the debate yesterday.

14 Thank you very much. I think, Ms Dunlop can now
15 proceed.

16 MS DUNLOP: Thank you, sir.

17 THE CHAIRMAN: It's Professor Lowe, is it?

18 MS DUNLOP: Yes.

19 PROFESSOR GORDON LOWE (continued)

20 Questions by MS DUNLOP

21 MS DUNLOP: We have Professor Lowe with us again this
22 morning to give evidence to topic C3A. Since we are
23 today moving from our introduction on hepatitis topic
24 into this particular, slightly different topic, perhaps
25 I can just read the terms in which the topic has been

1 expressed.

2 The use of blood product concentrates in Scotland in
3 the period between the introduction of NHS heat-treated
4 products in 1984 and the supply of NHS products
5 sufficiently treated to inactivate Hepatitis C, which we
6 know to have been in around the spring of 1987.

7 So it's really that little period that we are
8 looking at now.

9 Professor Lowe, you have provided the Inquiry with
10 a statement on this topic and we should have that on our
11 screens. It's [\[PEN0171471\]](#). You remind us of your own
12 personal position between 1985 and 1987. You were at
13 that point a consultant physician in the university
14 medical unit at Glasgow Royal Infirmary, although you
15 also continued to have academic responsibilities.

16 You tell us that you shared consultant
17 responsibility for the care of haemophilia patients with
18 Dr Forbes, but you go on to record that Dr Forbes, as
19 haemophilia centre co-director, was in charge of the
20 centre's administration and policy and attended the
21 meetings of UK haemophilia reference centre directors
22 and other haemophilia administrative bodies, until he
23 moved to Dundee in 1987, at which point you succeeded
24 him as haemophilia centre co-director.

25 You undertook that role jointly with

1 Dr George MacDonald initially and then from 1990 with
2 Dr Isobel Walker.

3 You respond to our first question, which concerns
4 the level of awareness among treating haemophilia
5 physicians in this period, that the Scottish NHS product
6 was less effectively treated against non-A non-B
7 Hepatitis than what was available in England.

8 Your answer, Professor Lowe, is that you remember
9 that from 1986 -- you are not sure when -- Dr Forbes
10 told you that the current Factor VIII concentrate --
11 that was the Scottish Factor VIII concentrate -- might
12 not be effective against non-A non-B Hepatitis. I think
13 it's perhaps just the way it's worded, Professor Lowe,
14 because you are presumably not suggesting to us that
15 that's the first time you had realised there was a risk?

16 A. No, by no means. I think the preamble probably should
17 have been that, as I recall, heat treatment was
18 introduced at the end of 1984, really because of HIV.

19 Q. Yes.

20 A. Which is very susceptible to heat treatment, as I think
21 the Inquiry knows, and that was the rationale for
22 introducing heat treatment in Scotland. And I think at
23 that time it was realised that while progressively
24 increasing degrees of heat treatment might in the future
25 protect against non-A non-B Hepatitis, there was no

1 assurance when heat-treated factors were introduced into
2 Scotland, or indeed anywhere else, that that would solve
3 the problem of non-A non-B Hepatitis.

4 I think what then happened during 1996 [sic - 1986]
5 was that there was increasing evidence from studies of
6 other products, which were heat-treated to a similar
7 extent as the SNBTS product, that indeed cases of non-A
8 non-B Hepatitis were still occurring. And it was the
9 inference then during 1986, and I think the evidence was
10 obviously discussed at the meetings that Dr Forbes and
11 Dr MacDonald attended, meetings of the UKHCDO and the
12 Scottish directors with transfusion colleagues, that
13 certainly one could still not make any guarantees to
14 patients that that degree of SNBTS heat treatment would
15 be effective against non-A non-B Hepatitis.

16 Why I mention 1986 is that, obviously, it was quite
17 customary for the unit as a whole to sit down regularly
18 and discuss policies. I do recall that Dr Forbes told
19 me at some time during 1986 that, because of the
20 increasing evidence that the current SNBTS products
21 could not be guaranteed to reduce the risk of non-A
22 non-B Hepatitis, his policy, together with Dr MacDonald
23 and Dr Davidson, was to continue the unit's policy that
24 those patients most at risk, which is patients with no
25 previous exposure to clotting factor concentrates, or

1 very minimal, should continue to be treated with
2 alternative products, for example cryoprecipitate for
3 patients with moderately severe Haemophilia A or
4 von Willebrand's disease. And the rationale for that,
5 as I have said in the statement, is the much smaller
6 donor pool with cryoprecipitate, perhaps 20 donors,
7 compared to the thousands for a factor concentrate.

8 Q. Professor Lowe, before we go too far into 1986, can we
9 go back to December 1984, because I wanted to begin our
10 examination of this period just by looking at what was
11 said by the reference centre directors in December 1984,
12 and that will enable us, I think, then to move forward
13 further on to the period that you are telling us about.

14 The reference centre directors did meet
15 in December 1984, I think on the 10th, and we know that
16 Dr Forbes was at that meeting as a representative of
17 Glasgow.

18 Could we look at document [\[SGF0012388\]](#), please?

19 This is a guidance document which emanated from that
20 meeting, so this is from December 1984, and we can see
21 that the first page is giving a little bit of background
22 about the current difficulties, and if we scroll down,
23 we can see there is mention of the availability of
24 tests, diagnostic testing, general precautions. Then on
25 to the second page. We can see a heading

1 "Concentrates", and there is a little resume of the
2 current picture as far as heat treatment is concerned.
3 And we see, in the fourth line of the section dealing
4 with Factor VIII, the statement that it is unlikely that
5 this process -- that's the dry heat treatment -- in
6 fact, what's been referred to as "dry heat treatment at
7 68 degrees for 24 hours":

8 "It is unlikely that this process completely
9 inactivates non-A non-B Hepatitis."

10 Then a little bit of discussion of wet heat. The
11 following paragraph talks about Factor IX and the
12 availability of some commercial products there, and then
13 BPL Factor VIII and Edinburgh. Then, if we go down to
14 the options, we can see that this document lists options
15 in probable decreasing order of safety from AIDS for
16 Haemophilia A:

17 "1. Heated UK concentrate. Note: still NANB
18 hepatitis risk."

19 Then:

20 "Single donor cryo or fresh-frozen plasma.

21 "3. Heated imported concentrate. Note: still NANB
22 hepatitis risk."

23 Then:

24 "Unheated UK concentrate and unheated imported
25 concentrate."

1 Then there is another note:

2 "Heated concentrates may still transmit hepatitis.
3 Some of the distinctions, for example, between 3 and 4
4 are debatable and the long-term effects of using heated
5 plasma proteins in this way are unknown. Even
6 pasteurised albumin is not given as frequently to
7 individuals as will be Factor VIII."

8 We understand what these concerns are directed at,
9 that there was a worry in this period about neoantigens,
10 for example. So we understand that. Then
11 recommendations that concentrates still needed:

12 "Use DDAVP in mild Haemophilia A and
13 von Willebrand's disease if possible."

14 Then on to the next page:

15 "For Haemophilia A needing blood products, virgin
16 patients, those not previously exposed to concentrate
17 and children, use cryo or heated NHS Factor VIII, if
18 available."

19 Then:

20 "Severe and moderate haemophiliacs previously
21 treated with Factor VIII, use heat-treated NHS Factor
22 VIII if available or heat-treated US commercial."

23 Then similar sorts of recommendations for
24 Haemophilia B, fresh-frozen plasma, and then for virgin
25 patients:

1 "Fresh-frozen plasma or NHS Factor IX concentrate if
2 essential. Severe and moderate Christmas Disease
3 previously exposed, continue to use NHS Factor IX. In
4 individual patients there may need to be a choice."

5 And so on. Just to let everyone have a look at that
6 paragraph. (Pause)

7 Professor Lowe, I'm wondering if you remember
8 Dr Forbes coming back from the meeting or receiving this
9 guidance through the post and sharing its contents with
10 you?

11 A. Oh, yes, I was -- Dr Forbes, certainly in December 1984,
12 spoke to the whole unit about the introduction of heated
13 SNBTS products and that was what was used. He certainly
14 reviewed the different categories of patients, and as
15 far as I can recall, the unit policy was very much in
16 accordance with these recommendations.

17 Q. There does seem to be a clearly expressed understanding
18 in this that there continued to be a risk of non-A non-B
19 Hepatitis.

20 A. Yes.

21 Q. And I just wondered, particularly, I suppose, given your
22 reference to 1986, what the position had been
23 between December 1984 and 1986. What was the picture in
24 Glasgow? What was the understanding as to what
25 treatment should be given?

1 A. Well, very much in line with what you see there on the
2 screen. The majority of our patients requiring factor
3 concentrates were severe haemophiliacs. They had been
4 treated for many years with Factor VIII concentrates.
5 That was what they continued to have, and while patients
6 could be told that the heat treatment was thought likely
7 to reduce the risk of HIV, there was no evidence at the
8 time that it would reduce the risk of non-A non-B
9 Hepatitis. Hence, in patients who had not been
10 previously exposed to concentrates, the desirability to
11 try, as I have said, to limit the exposure to non-A
12 non-B Hepatitis by considering the use of alternative
13 products, cryoprecipitate or fresh-frozen plasma,
14 according to individual circumstances.

15 Q. Yes. You see, if we look, for instance, at that passage
16 at the top of the page under the numbered paragraph 3,
17 it says:

18 "For virgin patients, those not previously exposed
19 to concentrate and children, use cryo or heated NHS
20 Factor VIII."

21 That's quite a choice: cryoprecipitate or heated NHS
22 Factor VIII, because we saw from the previous page --
23 can we just flip back to that, please? -- the mention,
24 under the heading "options", of the continuing risk of
25 non-A non-B Hepatitis in association with heated UK

1 concentrate.

2 A. Hm-mm.

3 Q. And then the second suggested option, single donor cryo,
4 doesn't bear a similar caveat. So I suppose I'm trying
5 to tease out from you what in Glasgow was the preference
6 as between those two: cryoprecipitate or NHS heated
7 Factor VIII?

8 A. As I recall, the majority of our patients had the heated
9 SNBTS Factor VIII concentrate. There were a small
10 number of patients who had not previously received
11 concentrate and for those, if one was particularly
12 concerned about non-A non-B Hepatitis, then
13 cryoprecipitate or FFP, for patients with Factor IX
14 deficiency, might be preferable.

15 I recall that Dr Forbes's policy was very much to
16 consider the individual patient. We didn't have many of
17 these patients. An additional complication with
18 von Willebrand's disease is that Factor VIII concentrate
19 may not be effective in preventing bleeding in
20 von Willebrand's disease, and for those patients, cryo
21 was preferable because it contained high amounts of
22 von Willebrand factor.

23 So I think Dr Forbes's policy was very much to say,
24 "Let's look at these small number of patients on an
25 individual basis, look at their previous history of

1 bleeding, distinguish between haemophilia and
2 von Willebrand's disease, look at the haemostatic
3 challenge that was forthcoming" -- because many of these
4 moderately affected patients, you are talking about only
5 the occasional tooth extraction every few years or
6 occasional other type of surgery or a traumatic episode,
7 and then to make a judgment on that.

8 I think the other factor, of course, with HIV was
9 that HIV testing of blood donors came in during 1985,
10 from memory.

11 Q. Yes.

12 A. And there may well have been some reluctance to use
13 cryoprecipitates until the blood donors were all tested
14 for HIV because of the potential risks of HIV.

15 But my recollection is during this whole period of
16 the end of 1984/85, into 86, the directors had to
17 continuously weigh up what was happening and many
18 circumstances. HIV testing of donors and then to
19 consider for the individual patient, in the individual
20 circumstance, what was the safer product. And I recall
21 that Dr Forbes was very active in speaking to these very
22 small number of patients in whom the choice could be
23 made. He had known them man and boy, you know, and was
24 very well acquainted with the patients and their
25 individual problems and would have careful discussion as

1 to what the choice would be.

2 Q. Right. Thank you, Professor Lowe.

3 You have covered a number of different important and
4 interesting issues. During that period, small as it is,
5 84 to 87, we know that there were some significant
6 changes and the introduction of screening of donated
7 blood in October 1985 is clearly one of those. If the
8 whole exercise is seen as a balancing one, then
9 obviously the knowledge that all donations were being
10 screened for the AIDS virus would alter the balance, and
11 I think we can understand that. You know, it makes
12 blood, and presumably cryoprecipitate, appear safer than
13 it had previously.

14 I'm still interested in that sentence at the top of
15 the next page about the choice between heated NHS
16 product and cryoprecipitate. We appreciate from what
17 you are telling us that numerically speaking, the vast
18 majority of the patients in Glasgow Royal Infirmary
19 would be on heated NHS Factor VIII, and I think we
20 understand the reasons for that. So what sort of
21 patient would be in the minority and would present the
22 dilemma of choosing between heated NHS Factor VIII and
23 cryo? Can you just explain that a little more for us?
24 What sort of patient are you going to be scratching your
25 head over?

1 A. The sort of patient I have in mind, and my mind going
2 back 25 years, I have to say, finds it very difficult to
3 think who were these people, how many were there.

4 Q. Yes, indeed.

5 A. And because of the very difficult choice -- I mean,
6 I had become a consultant in October.

7 Q. October 1985, I think you have told us.

8 A. Thank you.

9 Having said that, Dr Forbes had years more
10 experience in haemophilia and knew the patients much
11 better than I had. And that kind of patient, I didn't
12 personally struggle much with because that was very much
13 a decision that Dr Forbes wanted to make. So my
14 recollections were very few patients. I struggle to
15 remember individual instances but in general, for
16 patients with moderate severity Haemophilia A, who had
17 never had concentrate before, they might have had just
18 maybe two or three exposures to cryoprecipitate
19 previously, for example every five years for a dental
20 extraction.

21 My recollection is none of these patients has ever
22 had symptomatic or asymptomatic hepatitis and therefore
23 they could perhaps be assumed, given the diagnostics at
24 the time, to have escaped hepatitis. Then you have the
25 choice between a product which, while heat-treated, the

1 heat treatment is, you know, insufficient to prevent
2 non-A non-B Hepatitis. We know from UK studies -- well,
3 English studies in 1983 and 1985 -- the reference is,
4 I'm sure, available to the Inquiry -- that prior to the
5 introduction of heat treatment, it was virtually
6 100 per cent risk that you would get non-A non-B
7 Hepatitis from the serial studies. That was very much
8 in people's mind. So you then have the balance between
9 a patient with moderate severity Haemophilia A,
10 infrequently treated with cryoprecipitate, their
11 previous exposures to cryoprecipitate have prevented the
12 serious bleeding that can occur after a tooth
13 extraction, surgery, whatever, the patients are familiar
14 with the product and you then have to say to them,
15 "Well, you know, there is a choice. You can have
16 a product which, while heat-treated, the concentrate,
17 it's coming from thousands of donors and there is no
18 guarantee that you will not get an episode of non-A
19 non-B Hepatitis, which you don't want." And
20 particularly after the introduction of HIV testing of
21 blood donors, cryoprecipitate, you know, while it could
22 still have a small risk of HIV, had a very good safety
23 compared to concentrate, a reduced risk of getting
24 hepatitis.

25 So those, I think, would be the kinds of discussions

1 that would go on. Given that most of these patients you
2 are talking about, elective procedure, the dentist
3 contacts you and says, "I want to extract four wisdom
4 teeth," that would allow plenty of time for
5 consideration between the choice of the two products and
6 obviously discussion with the patient.

7 If I could just turn from Haemophilia A to
8 von Willebrand's disease, the extra factor I have
9 alluded to already with von Willebrand's disease is that
10 the concentrate might not be effective because it's not
11 replacing the von Willebrand factor, and therefore an
12 additional reason for preferring cryo in that kind of
13 patient who comes up for a tooth extraction is that you
14 are more assured of achieving haemostasis.

15 Q. You have been alluding to patients with moderate
16 haemophilia. Would it be right to think of patients
17 with mild haemophilia as being, as it were, an even
18 stronger case of individuals who present this dilemma;
19 so somebody with mild haemophilia but who perhaps is
20 having a bleed or is destined for some kind of procedure
21 for which they need some sort of cover.

22 The first thing that you have said -- and you have
23 said this several times -- is what you would tell the
24 patient. Are we to take it then that in Glasgow, in the
25 Royal Infirmary, in this period, the patients were

1 involved in the decision-making?

2 A. Oh, yes.

3 Q. Right. So you would be frank with the patients about

4 the nature of the risks, both the hepatitis risk and the

5 HIV risk?

6 A. Yes, I think when I appeared here previously, one of the

7 first questions I was asked was, "Since you joined the

8 haemophilia unit in the 70s, was non-A non-B Hepatitis

9 discussed with patients?" and the answer is yes, it was

10 very much part of the unit's policy to recognise

11 that there was a risk of hepatitis and to share that

12 with the patients.

13 Q. And --

14 A. To go back to mild haemophilia, obviously the treatment

15 of choice from about 1980 was desmopressin, and we were

16 very rigorous in assessing all newly diagnosed patients

17 with mild haemophilia; they all routinely had

18 desmopressin infusions. The majority of those would

19 have a predictable response from Factor VIII and you

20 could therefore say to those patients, "You have got

21 mild haemophilia. If have an injury or if you have to

22 have surgery, this is the product we will use, and

23 hopefully that will allow us not to ever use blood

24 products on you." For patients with mild Haemophilia A

25 and for patients with mild severity von Willebrand's

1 disease. And that, in conjunction with ancillary
2 haemostatic measures, like tranexamic acid, would be the
3 treatment of choice, and I really cannot remember in
4 this period of time, which you are asking about, 1985 to
5 1987, any patients in the category of mild haemophilia
6 and von Willebrand's disease who had to have a blood
7 product, for example, due to failure of desmopressin and
8 tranexamic acid. So that was very much the policy for
9 that quite large group of patients with mild
10 haemophilia.

11 Q. You will correct me if I am wrong about this but I think
12 I can imagine that the easiest situation for you to be
13 dealing with at that time would be the patient with mild
14 haemophilia who is having a planned intervention of some
15 sort.

16 A. Yes.

17 Q. Because everybody has time to organise the DDAVP or
18 something like that.

19 Let's ratchet it up slightly and ask about the
20 patient with mild haemophilia but who is having a bleed.
21 What was the thinking in Glasgow about that sort of
22 patient in this era?

23 A. Most of the time desmopressin was effective. It gives
24 you a transient increase in Factor VIII and
25 von Willebrand factor, which is usually enough to sort

1 out the problem. In addition, if you look at the
2 biology of Factor VIII and von Willebrand factor, if you
3 have an injury or trauma, that leads to what we call
4 an acute phase response, where the level of certain
5 proteins in the blood increases, including Factor VIII
6 and von Willebrand factor.

7 In a sense, even if desmopressin's effect is limited
8 to 48 hours, after 48 hours, we, sitting in this room
9 with, say, 100 per cent Factor VIII and von Willebrand
10 factor levels, would have gone up to 200 per cent, and
11 a mild haemophiliac, say, going along about 10 or
12 20 per cent would have gone up to 30, 40, 50 per cent,
13 which is approaching the levels required to achieve
14 normal haemostasis. So the response to injury, response
15 to surgery, in itself often made the mild haemophiliac
16 almost into a normal range for haemostasis.

17 So what I'm saying is that, even after a bleed, the
18 combination of desmopressin and the response to injury,
19 which is present in haemophiliacs and vWD patients as
20 well as the normal population, usually allowed one to
21 not have to give blood products.

22 In the event that somebody had a major bleed or
23 major surgery and this combined treatment would then
24 result in the patient continuing to have major bleeding,
25 a discussion would have to take place with the patient

1 about the risks of blood product treatment: "You are
2 keen that we stop your bleeding. We are keen to help
3 you, but you will have to recognise that if you are an
4 infrequently treated patient, your first exposure to
5 concentrate has a high risk of giving you non-A non-B
6 Hepatitis, and even if we give you cryoprecipitate, you
7 know, if we have to give you a large dose of
8 cryoprecipitate for several days, that, again, is
9 building up to a risk of non-A non-B Hepatitis, given
10 the prevalence of the virus in the population that we
11 now know."

12 Q. This is a hypothetical patient and we can create for
13 ourselves certain difficulties with hypothetical
14 patients, but sticking with the concept for the moment,
15 this hypothetical patient is in a difficult situation
16 because they are unwell and they are having explained to
17 them two possible choices, neither of which is
18 completely safe or even particularly attractive, that
19 they could have cryoprecipitate, which might give them
20 the AIDS virus, or they could have NHS heated
21 Factor VIII, which is safer than unheated Factor VIII
22 because of the treatment against the AIDS virus, but
23 which carries still a risk of hepatitis.

24 As doctors, you must have been giving them some sort
25 of steer. What sort of a steer would it have been?

1 A. Well, as I say, these patients were infrequent.

2 Q. Yes.

3 A. And I cannot remember, as an individual, having to make
4 this decision, like, in the middle of the night.
5 Dr Forbes knew the patients well, had very up-to-date
6 information and I think in that situation he would be
7 seeing the patient --

8 Q. I'm going to quibble with you, Professor Lowe, because
9 this patient is a mild patient. So an infrequent
10 visitor and not somebody particularly well-known to
11 Dr Forbes. So let's just change that little bit of
12 hypothesis. What sort of a steer do you think would be
13 given to the patient? I appreciate it's very difficult
14 to recall and you are trying to reconstruct something
15 you can't remember ever actually personally having to
16 deal with. With those caveats, do you think there was,
17 in Glasgow Royal Infirmary, a sort of a preferred
18 solution?

19 A. Well, if it was me in the middle of the night and
20 Dr Forbes is in Hawaii or something, so it's up to me
21 making a decision in such a patient, what I would do in
22 that theoretical case is to say, "We have guidelines at
23 a national level in the UK, we have a choice of
24 products. At the end of the day, you and I, here and
25 now, have to make a decision between cryoprecipitate or

1 a concentrate." I would go through the risks and
2 hopefully, you know -- it depends on the exigencies of
3 the situation -- and say, "Well, there is HIV and there
4 is non-A non-B Hepatitis," and lay it out with them. My
5 approach as a doctor, as I think I said the last time
6 I sat in this chair, has always been to try and give
7 them my summary, as a doctor, of the best evidence and
8 to then work with them to make a decision. At the end
9 of the day, if the patient says, "It's up to you,
10 doc" --

11 Q. "What would you do, doctor?" That's what patients say.
12 They say that to lawyers too, they say, "What would you
13 do?"

14 A. You are absolutely right. And my position has always
15 been, if we reverse positions and I'm the patient lying
16 in that bed with the bleed, what would I choose, just
17 based on my knowledge and if it were me. And you are
18 now going to ask me what I would say --

19 Q. I think we are actually on the edge of our seats,
20 Professor Lowe.

21 A. You think you are on the edge of your seat; I'm even
22 more so.

23 It's interesting. I think -- and you are talking
24 about what period of time?

25 Q. Let's make it slightly easier and let's take it

1 post-October 1985?

2 A. When people are HIV tested?

3 Q. Yes.

4 A. I would say to myself, right, I have a bleed which is
5 not stopping. If I have cryoprecipitate for 20 donors
6 who are HIV tested, I would take that.

7 Q. Right. Thank you.

8 It feels like a long time since we were looking at
9 your statement, so let's look at it again.

10 THE CHAIRMAN: Let's not go there just too quickly.

11 I have to say, I have a certain concern about just
12 how realistic this scenario is. The patient who comes
13 in in dire need of treatment is not going to be the most
14 rational person in some cases, and the notion of getting
15 a lecture on the comparative advantages and
16 disadvantages of forms of therapy perhaps might be
17 rather lacking in reality in some cases.

18 I'm wondering whether in fact the only question that
19 would be of interest to the patient was, "Doc, what do
20 you want? What would you do for me?" And you see, that
21 would be the positions that would put the doctor at
22 maximum risk. He is then being asked to take the
23 responsibility.

24 In those circumstances, would you not just accept
25 the responsibility and say, "The best way of dealing

1 with your case today, now, is X"?

2 A. Yes.

3 THE CHAIRMAN: Did you really give a lecture? Think of the
4 amount of time we have spent here trying to get to
5 understand these factors and we may not have reached
6 there yet, Professor Lowe. Did it really happen, you
7 know, as a matter of fact -- let's get down to the
8 realities. Did it really happen that there were these
9 long lectures or was it much more stark?

10 A. Well, sir, I'm a lecturer and have been since 1978.

11 THE CHAIRMAN: That's no excuse.

12 A. I tend to lecture, and sitting here looking at me, you
13 think, "This man is giving us a lecture," but I'm just
14 trying to distil for the Inquiry what I would have done.

15 No, of course. If it's two in the morning and you
16 are at the patient's bedside, you have to make
17 a decision, you have someone with urgent bleeding and
18 you need to order something in the next ten minutes,
19 I would not sit and give them a two-hour lecture, no,
20 sir. What I would do is try and encapsulate, in the
21 patient's own language and understanding, that there is
22 a choice, and I think it would be bad as a doctor if you
23 didn't tell them there was a choice, and then to say,
24 "There is this and there is that," wait for a bit and
25 then, if they said, "Right, I don't care, you do what

1 you think best," and then just give them what you would
2 give yourself.

3 MS DUNLOP: Yes. Thank you, Professor Lowe.

4 We should return to your statement, [\[PEN0171471\]](#).

5 As is apparent, we are on the second page. We have
6 covered some of this already, Professor Lowe. The
7 second question concerns just those very matters:
8 treatment policy for patients with haemophilia in that
9 period.

10 I think your explanation, certainly in
11 paragraph 2.1, is really as you have said, save for the
12 additional information which you have provided this
13 morning about particular hypothetical scenarios.

14 Would I be right in thinking from the tone of your
15 answer that in this conversation with the patient who is
16 having a bleed and is needing treatment, your default
17 setting is that you are trying to avoid the use of
18 concentrate?

19 A. Well, I think we were aware in 1985 that unheated
20 concentrate would give you non-A non-B Hepatitis. So
21 all the evidence was, from all round the world,
22 including the UK, that that was happening.

23 And to my knowledge there were no serial studies in
24 any Scottish patients like were conducted in England,
25 the other one, you could assume that that would apply to

1 the SNBTS concentrates.

2 I think also, remember in 1985 that the consensus
3 was, until about that time, that "non-A non-B Hepatitis"
4 was a relatively benign disease, given that after years
5 of treatment, you know, you were not seeing patients
6 with clinically severe liver disease. That perception
7 started to change, I think about 1985, with reports from
8 Dr Hay's group in Sheffield and others, if you were
9 brave enough to do biopsies in numbers of haemophiliacs,
10 you could see more severe changes in the liver
11 histology, and therefore there was an increasing concern
12 that you should do everything you could to prevent that
13 first episode of non-A non-B Hepatitis.

14 So I think there was awareness that heat treatment
15 was initially not effective, that non-A non-B Hepatitis
16 was more or less inevitable if you got concentrate, and
17 that there was increasing evidence that that could lead
18 over the patient's lifetime to an increased risk of
19 liver disease. So I think haemophilia treaters
20 generally were, you know, very keen to avoid
21 concentrates, to try and use desmopressin and other
22 measure if possible, and then to seriously consider, in
23 this small number of patients with moderate severity
24 haemophilia and vWD, the use of cryoprecipitate. Does
25 that answer your question?

1 Q. Yes, I think so, thank you.

2 2.2 goes on to address Factor IX.

3 THE CHAIRMAN: Before you go to it, one question, another
4 question of fact: you became consultant in 1987 but no
5 doubt you were very -- sorry, director.

6 A. Director at the end of --

7 THE CHAIRMAN: No doubt you were very much aware of what was
8 going on before. Did you have any impression of the
9 proportion of patients in each or any of the classes,
10 severe, mild et cetera, who had NANB hepatitis at that
11 stage in your group?

12 A. In the group of patients attending Glasgow Infirmary,
13 there were certainly a high percentage of patients who
14 had been treated with concentrates over the years, who
15 had occasional or persistent elevation in liver enzymes,
16 as was the case throughout the world.

17 THE CHAIRMAN: So you were doing the LFTs and all the rest
18 of it, regularly and had that information available.

19 A. Those were done routinely from, I think, the late 70s,
20 certainly the early 80s, and like every other centre in
21 the world, we found that a high percentage of previously
22 treated patients had intermittently or persistently
23 elevated transaminases.

24 THE CHAIRMAN: Was it a relevant factor in deciding as
25 between different courses of treatment that there was

1 information available about the individual patient
2 relating to the probable NANB status?

3 A. I think the group of patients, the small number of
4 patients, in whom the choices between cryoprecipitate or
5 concentrate for the first time -- I don't think that
6 really applied to that group of patients. As far as
7 I recall, they would have normal liver function tests,
8 and what you were trying essentially to do is to stop
9 that situation going into one where they might well have
10 chronic non-A non-B Hepatitis.

11 So the patients I'm talking about are the severely
12 affected patients who had had treatment with
13 concentrates in the past.

14 MS DUNLOP: What about the patient in the middle, the
15 occasional user? You have spoken about people with
16 moderate haemophilia and I suppose they might present
17 too and need treatment. They are not virgin patients
18 because they have had concentrate maybe once ten years
19 ago or something like that. In the circumstances that
20 the chairman is sketching, would you be looking to see
21 what are this person's LFTs?

22 A. Okay. Again I'm struggling to find an individual
23 patient but say you have two patients with moderately
24 severe haemophilia A and they are coming up for surgery
25 and desmopressin aint going to work and you are choosing

1 between cryoprecipitate or a first exposure to
2 concentrate. I suppose you could say that if that
3 patient, for whatever reason, had abnormal liver
4 function tests at some time, then that might cause you
5 to say, "Maybe we will just go for concentrate because,
6 however you got it, it's quite likely that you have had
7 non-A non-B Hepatitis before."

8 But remember that serum transaminases are
9 a notoriously non-specific indicator of hepatitis.
10 Working in Glasgow, alcohol was quite prevalent in our
11 patients, as in the non-haemophiliac population, obesity
12 was becoming a factor and you cannot really assume in
13 the 1980s, before, you know, Hep C testing, what
14 somebody's abnormal liver function tests are due to.

15 For example, as well as doing haemophilia clinics,
16 I did general medical clinics in the east end of Glasgow
17 and, you know, routine blood tests included abnormal
18 liver function, and every afternoon I would see half
19 a dozen new patients and write to the GP saying, "By the
20 way, the serum transaminases are up; check the
21 drinking."

22 Q. I think the chairman was perhaps thinking of that sort
23 of patient who is not a virgin, you know, a previously
24 untreated patient, but somebody who has maybe had
25 concentrate ten years ago on one occasion or something,

1 and I think perhaps in that circumstance it might be
2 that you would want to know how are this patient's LFTs
3 looking?

4 A. Yes, it's a reasonable question and, yes, if somebody
5 had definitely had abnormal liver function tests and he
6 didn't think it was due to alcohol, a reasonable
7 inference would be that that patient had already been
8 exposed to non-A non-B Hepatitis, whereas the patients
9 with perhaps persistently normal liver function tests
10 might make you say, "That might swing you towards
11 cryoprecipitate because they haven't yet got hepatitis."

12 So, yes, it would be a factor, and I think, as the
13 guidelines say -- the document you put up at the end of
14 1984 saying individual patients -- no guideline can ever
15 be for the blind obedience of fools; they are there for
16 the guidance of wise doctors. And within a guideline,
17 yes, of course, you have to consider the individual
18 patient and make an individual assessment.

19 Q. Yes.

20 THE CHAIRMAN: Yes. I still have some difficulty seeing how
21 the doctor resolves the problem. It is the occasionally
22 treated person who will, on that hypothesis, have been
23 exposed to risk in the past, but if the position were to
24 be that at the time you only had variable transaminase
25 records -- and they almost certainly would be

1 variable -- and these were not diagnostic of hepatitis,
2 another possibility might, in the case in question, be
3 obesity when you saw the person. Another one, if they
4 were from the east end of Glasgow and in the cohort you
5 have described, could be alcohol.

6 You have got one out of three possible causes of the
7 raised transaminase that might indicate prior exposure
8 and therefore infection. How you are going to decide
9 which risk to take becomes a factor. We are not dealing
10 now with Koch's Postulates and mathematical certainty or
11 anything else; we are dealing with balance of
12 probabilities. So how do you deal with it?

13 A. It's very difficult in an evidence-free zone, in the
14 days before Hepatitis C testing was available. You
15 know, you look at the clinical -- you look at the
16 patient's history. Within moderately severe
17 haemophilia, there are people who bleed more than
18 others. It's a big spectrum. You would start with
19 that. You would then look at the haemostatic challenge
20 that the patient was about to face, like the severity of
21 the surgery. You would enquire about previous bleeding,
22 after dental extractions or whatever. You would enquire
23 about the family history, siblings with similar
24 deficiencies, what has their experience been, because
25 it's not just the level of Factor VIII and Factor IX;

1 there is individual variability in bleeding.

2 So, on the one hand, the doctor has to weigh up the
3 likelihood that that patient will suffer, you know,
4 serious bleeding; on the other hand, you have to do your
5 best, with limited evidence, to assess have they had
6 previous exposure to hepatitis.

7 I suppose, if you think about this more and more, if
8 that person is an alcoholic, they are going to be at
9 greater risk of progression of liver disease if they get
10 hepatitis. So there are factors in the individual that
11 will determine not just their risk of being exposed to
12 the virus but what long-term consequences are there
13 going to be.

14 So what you are trying to do, as in any other branch
15 of medicine where you are considering a choice of
16 treatments, is weigh up the two factors.

17 That's a very long-winded answer. But, yes, it's
18 multi-factorial. At the end of the day I think you are
19 down to a gut feeling. You have the patient saying,
20 "You are the doctor, what would you do?" And you have
21 to do your best to assimilate the individual person's
22 risk of bleeding, risk of hepatitis or HIV and then give
23 them your best, honest answer as a doctor, and that
24 usually is what would you want yourself.

25 Q. Yes. Can we just look at 2.2? As you say, this has

1 been mentioned before but from April 1985, as far as
2 Factor IX was concerned, there was a decision to use
3 commercial heat-treated product until SNBTS product
4 became available, as it was destined to do in the
5 autumn.

6 Question 3 was on a slightly different matter,
7 whether any of the hepatitis-safe products supplied in
8 England were made available to Scotland before May 1987,
9 and you told us that you looked at your statistics and
10 appendix 1 and also the use of commercial Factor IX in
11 the table and then FEIBA. But you say you can't see in
12 the table any other use of other Factor VIII products
13 and you can't recall any being used. So in Glasgow, in
14 the Royal Infirmary, you didn't use any product from
15 England?

16 A. Well, I cannot remember any being used. I think, at the
17 Inquiry's request, I was asked some months ago to
18 clarify, after Dr Forbes's evidence, the types of
19 product that were used during this time period. So
20 I can think of no better place than to go back to the
21 Inquiry's preliminary report, go through the table and,
22 to try and help you, work out, supplementing my memory,
23 as to what kind of products might have been used. I
24 cannot see in that table, as I have said in my
25 statement, any use of the English product 8Y and I

1 cannot recall any being used. It's maybe that
2 colleagues in England -- well, as far as I recall,
3 England was not self-sufficient in their heat-treated
4 products and something like only one third of patients
5 in England were able to have that and the rest were
6 still using commercial Factor VIII and, as you know,
7 Scotland was ahead of the game compared to other UK
8 countries in terms of self-sufficiency, and indeed with
9 heat treatment of the Scottish product, due to the
10 efforts of colleagues in SNBTS.

11 While, I suppose, it is possible that the English
12 product, being heat-treated to a higher degree than the
13 Scottish one, might have been an option for the
14 occasional patient with moderate severity Haemophilia A
15 being exposed for the first time to concentrate, I can't
16 recall any being used. It doesn't appear in the
17 Inquiry's table and it may well be that during that
18 period of time, between the English product being
19 thought on some preliminary evidence, as I recall, in
20 1986 to have a potentially lower risk of non-A non-B
21 Hepatitis, that might have been an option for an
22 individual patient being exposed for the first time.

23 It could well have been that during that period of
24 time, 1986 to 1987, before the SNBTS fully heat-treated
25 product appeared, we had no such patient having surgery.

1 Q. Right. Let's just learn a little more about the
2 position in England. Can we look at [\[DHF0030476\]](#),
3 please?

4 This is a BPL information sheet from July 1985 and
5 it relates to a new Factor VIII concentrate known as 8Y,
6 which is going to replace the intermediate specific
7 activity products with instantly forgettable names:

8 "General issue will begin from September 1st 1985."

9 Can we go a little bit down? We can see that the
10 heating protocol for this product is 80 degrees for
11 72 hours to reduce the risk of infection by viral
12 agents. What's interesting is the statement that:

13 "Safety and efficacy trials of the 8Y concentrate
14 are already proceeding at several haemophilia centres as
15 of 1 July 1985. Eight patients receiving 14 infusions
16 of three batches of concentrate have shown dose
17 responses in the range 1.1 to 2.9 and a mean half
18 clearance time of ten hours."

19 These are, I take it, acceptable, these statistics
20 for the dose responses and the mean half clearance time.
21 That sounds acceptable, does it?

22 A. In terms of getting the expected rise in Factor VIII?

23 Q. Yes.

24 A. Yes.

25 Q. Yes, okay. And then it goes on to say:

1 "Clinical trials at six haemophilia centres are in
2 progress to gain evidence of reduction or elimination of
3 viral transmission and several patients have safely
4 passed the point at which first evidence of NANBH virus
5 transmission would normally occur with unheated
6 Factor VIII."

7 So that's one snapshot. There are others from
8 England in 1985. That shows, I suppose, cautious
9 optimism about the new English product. Do you remember
10 hearing about this on the grapevine, people telling you
11 at meetings or in the department?

12 A. No, as I think I have made clear, I did not start going
13 to meetings of haemophilia directors until I became
14 a haemophilia director at the end of 1987.

15 Q. Right.

16 A. So I didn't go to these meetings. Dr Forbes,
17 Dr MacDonald, the co-directors in our centre did, and
18 while they would usually update me and other members of
19 the unit as to what was going on, in July 1985 I think
20 I was still a junior doctor. I became a consultant
21 in October that year and obviously, once I became
22 Dr Forbes's consultant colleague, he would probably
23 spend more time telling me about developments than when
24 I was one of his junior doctors.

25 But I cannot remember seeing that document

1 in July 1985, although I was aware that all
2 manufacturers of products with heat treatment or any
3 other virus inactivation procedure would very much want
4 to try and get that rare small number of patients who
5 had previously been not exposed to do serial studies of
6 non-A non-B Hepatitis.

7 Q. Yes. I mean, this is approaching the holy grail, isn't
8 it? A product that's severely heat-treated, so will
9 inactivate HIV and also, probably, the agent for non-A
10 non-B Hepatitis, and it works.

11 A. I'm not sure that you could make that interpretation
12 from the document that you are showing me because
13 I think it was about this time that the International
14 Society of Thrombosis and Haemostasis, under
15 Professor Mannucci, was setting up strict guidelines as
16 to how these studies should be --

17 Q. I take that absolutely, professor. I think I'm just
18 meaning it was good news and would it not have been at
19 least discussed or mentioned or referred to, Dr Forbes
20 saying to you, "Of course, you know that in England they
21 are moving forward with a severely heated product and,
22 you know, we would hope that in Scotland we will arrive
23 at the same result," or something like that? No?

24 A. I have no memory of that.

25 Q. Well, then, the next question is academic, because I was

1 going to suggest that it might have occurred to somebody
2 in the Royal Infirmary to try to get some from England.

3 A. It might have. I was lower down the food chain. I did
4 not interact regularly with haemophilia centre directors
5 in England. I mean, the first question, where you are
6 saying to me, during this period was there an awareness
7 amongst treating haemophilia physicians, that the
8 Scottish NHS product was in effect inferior to the
9 English product, well, the only haemophilia treaters
10 I spoke to across the country were Dr Forbes, my boss,
11 and Dr MacDonald. I did not go to haemophilia meetings;
12 I did not get the gossip, and I was not involved in the
13 policy-making or the selection of blood products. So
14 I'm not quite sure why I would have been involved in
15 those discussions.

16 Q. Well, fine, but even then just in retrospect, if we look
17 back on this situation and we imagine these hypothetical
18 patients we have already discussed, the person with mild
19 haemophilia who has a bleed and needs some treatment or
20 the person with moderate haemophilia, likewise needing
21 treatment, perhaps a very low exposure to concentrates
22 in the past, if there had been a small supply of the
23 English product in stock within the Royal Infirmary in
24 Glasgow, it would have been jolly useful for patients
25 like that, wouldn't it?

1 A. It might well have been but in 1985 I did not have this
2 information. That possibility was never discussed with
3 me.

4 Q. Or 1986?

5 A. I have no memory of that product being available to
6 Scotland in 1986. I was never told that.

7 Q. I suppose you don't know what's available until you ask,
8 but in 1986 -- let's then position this during a period
9 when you are a consultant -- you don't have any memory
10 of anyone proposing that you see if you could maybe get
11 a small supply of the English product?

12 A. No, none at all.

13 Q. Right. I think you are telling us it wouldn't have been
14 your job to have the idea; is that right?

15 A. Yes. I mean, what's the point? You have Dr Forbes as
16 chairman of the UKHCDO. He heads the viral safety
17 committee. He is in receipt of all the information
18 published and unpublished. Who better to make the
19 decision?

20 Q. Did you ever feel out of the loop?

21 A. I had plenty to do before I took over as
22 haemophilia centre director. Both Dr Forbes and I were
23 busy general physicians coping with all the acute
24 medical problems that the east end of Glasgow can throw
25 at you. That was the major part of our practice; the

1 50 per cent of our job that was NHS as distinct from our
2 big teaching and research loads, which are the
3 university ones.

4 When I became a consultant in October 1985, I sat
5 down with Dr Forbes and he said, "What do you want to
6 do? How are we going to do this?" I said, "Clearly you
7 need help with haemophilia and I'm very happy to help
8 you out with the administration of the haemophilia
9 unit," but it was very clear that Dr Forbes was running
10 it, it was his unit and I was his assistant.

11 My remit clinically, apart from general medicine,
12 was to try and develop thrombosis and vascular services,
13 which was my main interest. So I was developing a lot
14 of clinical research but also clinical services in,
15 venous thrombosis, in peripheral arteries and in stroke,
16 all orphan areas.

17 The cardiovascular disease that is Scotland's
18 biggest curse, that is ignored by cardiologists, who
19 deal only with the heart; that was my mission in life,
20 to develop vascular services for the east end of
21 Glasgow, where people were having strokes and thrombotic
22 episodes and dying like flies, and working very closely
23 with the diabeticians and the vascular surgeons to try
24 and improve the medical care of those patients.

25 I was developing those services and that was my

1 remit. And while I would discuss with Dr Forbes what
2 I was doing, that was my area of control, administration
3 and organisation.

4 He was very much the leader nationally, and in the
5 centre, of the haemophilia service. We were colleagues,
6 we collaborated but, you know, he had his business to do
7 with haemophilia and my clinical and administrative
8 interests were the other side of the
9 haemostasis/thrombosis equation. So I don't think it
10 was up to me, as somebody who was much junior to
11 Dr Forbes, Dr MacDonald and Dr Davidson and the Blood
12 Products Laboratory, who were very much leaders in the
13 fields of haemophilia, to interfere with their decisions
14 about policy.

15 Q. Right. Just lastly, Professor Lowe, I should remind
16 you -- you have probably looked at it again recently --
17 of your article in the Scottish Medical Journal, that
18 you published on these matters. It's [\[SNB0015523\]](#).
19 This is from 1987. I don't think it's very obvious to
20 us when in 1987.

21 A. I looked at this the other day and I think it was
22 published in August.

23 Q. I'm sorry, in August, did you say?

24 A. Hm-mm.

25 Q. Right.

1 A. I think if you look at the cover of the journal, it's
2 around August that year.

3 Q. Right, thank you. This is, I think, a more general
4 survey of the position as at that time, with, as it's
5 entitled, "Haemophilia Blood Products and HIV
6 Infection". It came out in the August 1987 edition,
7 roughly when would it have been written?

8 A. Oh, I think probably a few months before, probably about
9 the spring/early summer.

10 Q. Right.

11 A. I think the idea of this is that Dr Forbes, as editor of
12 the Scottish Medical Journal, and HIV and AIDS being
13 a topic suitable, he wanted an edition devoted to that,
14 largely for the education of medical practitioners
15 across Scotland, including general practitioners. So
16 this is one of a number of AIDS-related articles, and he
17 asked if I could review the situation of AIDS in
18 haemophilia with particular reference to the UK and to
19 Scotland.

20 Q. Right. Just if we could take a bit of a look at it, we
21 can see the abstract at the start. Then can we just
22 complete our scrutiny of the first page, which I think
23 is largely introductory. You point to the difference
24 between cryo and concentrate on the right-hand side:
25 "One therapeutic or prophylactic infusion of

1 cryoprecipitate comes from about 20 blood donors. One
2 infusion of lyophilised clotting factor concentrate
3 originates from several thousand blood donors."

4 In terms of incidence, you record that the majority
5 of concentrate-treated haemophiliacs were noted to have
6 intermittently or continuously elevated serum
7 transaminases after the introduction of clotting
8 concentrates. You say that:

9 "Recent serial studies have shown that hepatitis is
10 a constant finding after only one exposure to clotting
11 factor concentrate, and that the histological picture on
12 liver biopsy tends to worsen with time from normal or
13 chronic persistent hepatitis to chronic active hepatitis
14 or cirrhosis."

15 I think actually the reference there -- can we just
16 look at the last page? It's the editorial in the Lancet
17 which refers to some of the papers that we have been
18 looking at about incidence and severity.

19 Can we go back to the second page, please? You went
20 on to say that:

21 "On top of this morbidity and mortality from viral
22 hepatitis in haemophiliacs, has come HIV."

23 There is a bit of a discussion of AIDS, HIV and
24 AIDS. And then if you go down a little bit, please,
25 mention of current state, as far as infection is

1 concerned; prevalence in Scottish haemophiliacs, we can
2 see on the left. Then, I think, is that -- at the
3 bottom of the page, a little bit further down -- the
4 mention of what we tend to call the Edinburgh cohort, in
5 a passage on immuno-suppression by blood products. Then
6 you say you have shown that concentrate-treated severe
7 haemophiliacs had some altered immune responses. Then
8 another mention of Edinburgh:

9 "Progression of HIV in Haemophilia", which I don't
10 want to spend any great time on. Can we just move down
11 to the bottom of the page. Then "Preventive Measures
12 Against New HIV Infection."

13 You refer to the first preventative measure to the
14 selection of donors and then secondly to the heat
15 treatment of clotting factor concentrates since 1985.
16 Then if we go over on to the next page, we can see that
17 the third suggested measure is to use lower risk
18 treatments than clotting factor concentrates where
19 possible:

20 "This policy should also reduce the risk of viral
21 hepatitis, which is not prevented by heat treatment of
22 concentrates. Lower risk treatments include
23 cryoprecipitate ..."

24 Et cetera.

25 Professor Lowe, the heavy marking that we can see

1 here appears to have been applied in PFC in fact, and
2 there is a note that goes with this copy of the article,
3 expressing a view that the passage in the paragraph that
4 we can see on the left-hand side is dangerous, and
5 I think doing the best we can to reconstruct the train
6 of thought, the idea being that advocating any use of
7 unheated products, including cryoprecipitate, was
8 exposing people to a risk of HIV. I think that's the
9 point of view.

10 I just wondered, in the light of the discussion we
11 have already had at some length, if you want to respond
12 to that suggestion, that it would be dangerous to
13 advocate the use of these products, I think particularly
14 cryoprecipitate.

15 A. Well, could I ask you about this statement that it's
16 dangerous? Who did that come from and was it sent to
17 me?

18 Q. No, it wasn't. It's an internal -- like many documents
19 the Inquiry has come across, it's an internal comment,
20 and I think it's actually referred to in the preliminary
21 report, so you can go away and study it if you want, but
22 I think I'm really just interested in the point that
23 someone obviously strongly disagreed, a fractionator,
24 let's say, or somebody working in the --

25 A. Somebody making concentrates?

1 Q. Yes.

2 A. Yes.

3 Q. So someone very heavily involved in the heat treatment
4 of concentrates, who is, I suppose, taking an opposite
5 point of view.

6 A. Well, in that first part of 1987, as I recall, the
7 policy of the co-directors in Glasgow Infirmary was
8 still to consider in occasional patients not previously
9 exposed to concentrates, cryoprecipitate and FFP as an
10 option, as we have already discussed.

11 I accept that there is a variety of opinion about
12 that. If it's a colleague in SNBTS saying that current
13 heat-treated SNBTS concentrates are safe from viral
14 hepatitis, they do not have an evidence base for that
15 statement, because I clearly remember that the studies
16 of previously untreated patients in Scotland didn't
17 start until 1988. That was after I became
18 a haemophilia centre co-director. And while the report
19 of that study was finally published in 1993, showing,
20 within the limited number of previously untreated
21 patients that a small country of 5 million people can
22 assemble with great efforts by all my haemophilia
23 co-directors, particularly in paediatric centres, the
24 best evidence could be got that, that statement could
25 only be made in 1993. And with regards to your previous

1 statement about the English product was shown to be safe
2 in 1985, which I do not accept --

3 Q. I don't think I'm saying it was shown to be safe. I
4 think there were early indications that it might be
5 safe?

6 A. There was optimism by the manufacturer. Well, there
7 always is.

8 Could I remind you that it was not until 1993 that
9 the final report of the English previously untreated
10 paper was published at the same time as the Scottish
11 one. So I think it could be argued that if you are
12 looking at scientific evidence, it was 1993 before both
13 north and south of the border there was reasonable proof
14 of freedom from the risk of viral hepatitis.

15 Q. Yes.

16 THE CHAIRMAN: I think maybe we should have a break.

17 MS DUNLOP: I'm actually at the very end of Professor Lowe's
18 evidence. If it would be possible just to complete
19 that.

20 THE CHAIRMAN: Well, if you can.

21 MS DUNLOP: Yes.

22 If I were to suggest that Dr Perry had actually told
23 the haemophilia directors in March 1986 that BPL were
24 issuing a Factor VIII product, heated at 80 degrees for
25 72 hours, and preliminary data indicated that the

1 material was non-infective with respect to both viruses,
2 that would, I suppose, be a further instance of slightly
3 better founded optimism, if you like. So we looked at
4 something in 1985; by 1986 the picture is still good.

5 A. It may well have been, but I'm not party in 1986 to that
6 information. I don't go to these meetings with SNBTS or
7 other directors.

8 Q. And you wouldn't have been there? Right, okay.

9 Thank you very much, Professor Lowe.

10 THE CHAIRMAN: I want to come back to this question of
11 "I wisnae there" after the break, professor, but we will
12 have the break at this stage.

13 (11.07 am)

14 (Short break)

15 (11.39 am)

16 THE CHAIRMAN: Professor, we are all victims to some extent
17 of our own professional background and sometimes our
18 expectations are influenced by that, even if our
19 experiences aren't typical of others. But you see in
20 front of you examples of the sort of relationship that
21 I would expect among advocates. We have Ms Dunlop and
22 her team. We have Mr Di Rollo and Mr Dawson sitting
23 beside him, and you will see them exchanges information
24 and discussion all the time, to the extent that I think
25 I could say that mutual support in pursuit of whatever

1 happens to be the immediate interest almost characterise
2 the relationship of counsel. So it's perhaps not
3 unnatural for us to think that other professionals may
4 operate in the same way.

5 However, what you have tended to communicate to me
6 is a relationship between yourself and Professor Forbes
7 that in relation to a significant part of the work of
8 the hospital, really didn't involve that degree of
9 communication at all. I would expect Mr Di Rollo to
10 keep Mr Dawson fully engaged in what he was thinking,
11 and Ms Dunlop to keep the others in her team fully
12 engaged, and yet the impression that I get from some of
13 your evidence is that Professor Forbes attended all
14 these meetings, heard a great deal of information
15 because we have the minutes, but didn't communicate what
16 was happening to you.

17 That needs explanation, it seems to me. You may say
18 I'm totally wrong and I have misconstrued it but, you
19 know, my present impression is that there is a problem
20 there and I would like you to help me understand whether
21 there is a solution to it.

22 A. Well, thank you, sir.

23 Well, first of all, I should respond by saying that
24 obviously Dr Forbes and I were colleagues for many
25 years. We were friends socially, and I never had any

1 impression that there was a lack of communication
2 between us.

3 As I -- what I'm careful to say, I think, before
4 coffee, is that I was not a co-director at the time, I
5 did not go to any of these meetings, but I think I also
6 did say that, following these meetings,
7 Professor Forbes, particularly when I became a
8 consultant from October 1985, would invariably give me
9 a briefing as to what was happening in general, and in
10 particular as to whether there should be any change in
11 the policies, protocols or procedures of the unit. So
12 I would not wish you to infer, sir, that there was
13 a lack of communication.

14 What -- just when we finished before coffee,
15 Ms Dunlop was asking me about this possibility that 8Y,
16 the English product be used in Scotland, and I think
17 what I said was that I did not remember that as
18 a possibility. I'm not saying that that was not
19 discussed; it's just I cannot recall that.

20 But I'm wondering, sir, if there was any other
21 respect in which I have given you the impression that
22 we didn't speak to each other.

23 THE CHAIRMAN: I'm not going to analyse all of your evidence
24 here and now, but I may in due course, Professor, do so.
25 But it may be from what you say that I have got the

1 wrong end of the stick and, if so, that's unfortunate.

2 Ms Dunlop, I don't know whether you wish to follow
3 that in any way?

4 MS DUNLOP: No, I have no other questions, sir.

5 THE CHAIRMAN: Then we will go on.

6 Mr Di Rollo?

7 Questions by MR DI ROLLO

8 MR DI ROLLO: Yes, thank you, sir.

9 Professor Lowe, I wonder if I can ask you to look at
10 the preliminary report at paragraph 9.326, please.

11 When the topic was introduced today -- we are
12 dealing with a slightly different period, I think, but
13 I won't worry about that for present purposes. The
14 number of people treated for the first time in Scotland
15 with a blood product, during the period from
16 1 September 1985 to 30 June 1987, was 18 in the East of
17 Scotland and 13 in the West of Scotland. No doubt those
18 people would come in a number of shapes and sizes and
19 situations, but plainly that is a significant number of
20 people that decision-making, relative to treating with
21 a blood product during this period, would affect. Do
22 you agree with that?

23 A. Yes.

24 Q. And both in the East of Scotland and in the
25 West of Scotland -- I don't think there is any figure

1 there for the rest of Scotland or whether we are to take
2 it that the east goes all the way to the top of the
3 country et cetera, and the West likewise, but whether
4 there was anybody else in Scotland, but even leaving
5 that aside for the moment, plainly it is a significant
6 number of individuals being treated for the first time.

7 The concern that one has, obviously, in relation to
8 this matter is that treating someone for the first time
9 with a blood product during this period means that you
10 are exposing them to the risk of hepatitis -- non-A
11 non-B, as it was then known -- and that is something
12 which would be of concern to anyone administering -- or
13 should be of concern to anyone administering a blood
14 product during that period.

15 A. I agree.

16 Q. And would it be reasonable to say that one should not
17 give a concentrate unless it was unavoidable to do so,
18 given that there was that risk?

19 A. Yes, in general terms.

20 Could I just follow up your statement about these
21 patients coming in all shapes and sizes. I think "size"
22 is the relevant word here. I'm not sure about what
23 references 382 and 383 are but, as you are aware, we had
24 a previous Inquiry into hepatitis in Scotland about ten
25 years ago, conducted by the Scottish Office and

1 published. And I think at that time all haemophilia
2 directors were asked to look back at their patients
3 during the period of time that you mentioned and produce
4 data for that Inquiry as to how many patients at each
5 haemophilia centre were treated for the first time with
6 a blood product, and out of those 13 in the West of
7 Scotland, my memory is that the majority of those would
8 be children attending Yorkhill Hospital, the children's
9 haemophilia centre, because obviously it's as a child
10 that most patients with haemophilia get their first
11 exposure to a blood product.

12 I looked at that data recently and in our
13 Glasgow Royal Infirmary data, I think we only had about
14 three adult patients during that period of time treated.
15 So out of those 13, I think only about three patients
16 were treated for the first time in our unit at
17 Glasgow Royal Infirmary, which is what you would expect
18 for an adult haemophilia population.

19 Q. Can I ask you: as far as the Yorkhill ones, it's not
20 unusual for patients from Yorkhill to be referred from
21 other parts of Scotland, of course? Presumably the
22 children may well be referred there, it being a centre,
23 obviously?

24 A. Yes, so if a child in the West of Scotland, anywhere
25 between Carlisle and Stornoway, was diagnosed for the

1 first time or haemophilia was queried, they would be
2 referred to our paediatric colleagues at Yorkhill for
3 diagnosis and the initiation of treatment.

4 Q. I think we are aware, from information that we have,
5 that what you have told us about cryoprecipitate and
6 Yorkhill and the approach that was taken is that it
7 seems to be that cryoprecipitate would be a preferred
8 option because of the concern of non-A non-B Hepatitis
9 during this period?

10 A. Yes, I think that was what was recommended in the UK
11 national guidelines at the time. But obviously, you
12 would have to ask my ex-colleagues at Yorkhill about
13 that.

14 Q. Right. But getting back to what I was suggesting to
15 you, the position is that one would not give
16 a concentrate to a previously untreated patient unless
17 it was unavoidable, and I think you agree with that?

18 A. I agree.

19 Q. And just in very general terms, obviously, in looking at
20 the situation as it presents to the doctor, the first
21 thing a doctor has to do is to assess the situation and
22 work out what the specific problem is or may be before
23 one goes into any decision about what to do or not to
24 do. Is that fair?

25 A. Indeed.

1 Q. And in particular, one would have to determine what the
2 nature of the bleeding disorder was?

3 A. Yes.

4 Q. And find out exactly what the patient's deficiency may
5 or may not be?

6 A. Yes, of course.

7 Q. And the issue about a concentrate would only arise if
8 one has a situation or has information, which is
9 reliable information, that one has a Factor VIII or
10 a Factor IX deficiency or a von Willebrand's disease
11 problem.

12 A. That's what one would like.

13 Q. Yes, well, that's what should happen, isn't it? Is that
14 right?

15 A. Oh, yes, absolutely.

16 Q. The issue about whether you use a concentrate would only
17 arise if one decided that there was no alternative but
18 to use a concentrate therefore.

19 A. Correct.

20 Q. I think the suggestion has been put to you, and you have
21 indicated that you didn't play any part in the
22 decision-making process, but if English 8Y had been
23 available in this period in Scotland, a small supply had
24 been available, then consideration might have been made
25 that if you had got to the point at which you had no

1 alternative but to use a factor concentrate, in
2 a previously untreated patient you might decide, "I'll
3 use 8Y because it gives a better level of protection".

4 A. Yes, that might well be the case but, as I said before
5 coffee, I have no recollection of such a product being
6 in Glasgow Royal Infirmary or used in
7 Glasgow Royal Infirmary.

8 Q. I don't think we have any information that it was used
9 or was available and I think your position is that you
10 yourself had no involvement in any decision-making
11 process, but if 8Y had been asked for, then it might
12 then have become available and therefore might have been
13 used.

14 A. It might have been used, yes.

15 Q. Thank you. I have no further questions.

16 THE CHAIRMAN: Mr Anderson?

17 Questions by MR ANDERSON

18 MR ANDERSON: I'm obliged, thank you.

19 Professor Lowe, you were discussing with Ms Dunlop
20 the situation where the doctor had a difficult choice to
21 make and you had to weigh up the various factors
22 according to the circumstances of the patient; do you
23 remember that?

24 A. Yes.

25 Q. And you used the phrase, I think, "It's very difficult

1 because it's an evidence-free zone". Would I be right
2 in thinking that one of the factors that one would take
3 into account would be the anticipated treatment, in
4 other words the length of treatment, for example, the
5 number of doses one might require? Would that be
6 correct?

7 A. Yes, I think it would. For example, if you are thinking
8 about the choice between cryoprecipitate or the first
9 use of concentrate, an important question regarding the
10 bleeding episode is how bad is that bleeding. So, for
11 example, if somebody is exsanguinating or having a major
12 bleed into the brain, you would come to a stage where
13 you are thinking now, how much cryoprecipitate, if you
14 use cryoprecipitate, are you going to have to use; and
15 in either of these situations you might well be in the
16 case of giving, for example, daily cryoprecipitate for
17 two weeks to make quite sure that that bleeding was
18 arrested, in which case, any advantage about limiting
19 the donor pool by use of cryoprecipitate vanishes
20 because you are then exposing that patient to several
21 hundred donors, at which point any advantage over
22 cryoprecipitate for reducing the risk of non-A
23 hepatitis, relative to concentrate, becomes irrelevant.

24 So that kind of factor, what kind of bleeding is
25 occurring and thinking through not only the first

1 treatment that you give but how long that is going to be
2 given for, that's one example.

3 Q. So if it was anticipated that it might require, I don't
4 know, 10 to 20 applications, that would be something one
5 would take into account?

6 A. One would certainly consider that.

7 THE CHAIRMAN: And at the same time, of course, we tend to
8 think of cryoprecipitate as if it were a single unit,
9 but the reality might be that each day there would be
10 multiple units used. Up to how many?

11 A. Sorry, the average adult dose would be about 20 bags.
12 So that's 20 donors. It would vary according to the
13 patient's body weight.

14 THE CHAIRMAN: Yes, indeed. But it's possible to get
15 a wrong impression if one just thinks of cryoprecipitate
16 as a single-donor product. It hardly ever is.

17 A. Each bag is a single donor but you need to pool together
18 20 bags for the average adult. So if you then start
19 multiplying that over several days, weeks, or months,
20 you are approaching a significant donor exposure.

21 THE CHAIRMAN: Mr Anderson?

22 MR ANDERSON: I'm obliged, sir.

23 I think in your answer to me, professor, you used
24 the phrase "considering the choice between cryo on the
25 one hand and Factor VIII on the other hand," but in

1 answer to one of my learned friend, Mr Di Rollo's
2 questions, he put to you the issue of whether you use
3 concentrate only if there are no alternatives. I just
4 want to discuss this with you, if I may, because I have
5 some difficulty in reconciling that proposition with the
6 idea that there are circumstances in which one has
7 a choice, because earlier on I had understood you to say
8 there may be quite difficult decisions to make as to
9 whether to use cryoprecipitate on the one hand and
10 a concentrate on the other hand.

11 So am I not right in thinking that it's not quite as
12 simple as saying you never use concentrate if you have
13 an alternative? Because there are circumstances, aren't
14 there, where you have a choice -- a difficult choice to
15 make. Is that not right?

16 A. I think that's right, there is more of an equipoise for
17 a small number of patients between cryoprecipitate and
18 concentrate, as I think I was trying to explain before
19 coffee. You have to weigh up the lower donor pool of
20 cryoprecipitate against the larger number of donor
21 exposures using a concentrate but, as I have just been
22 saying, that will then depend on the number of
23 treatments that you have to give and what you may
24 consider exposing that patient to over a period of time.

25 Q. I'm obliged to you. Thank you very much, professor.

1 THE CHAIRMAN: While we are talking about choice, there is
2 one thing I ought to introduce, just to make sure that
3 it's here in the context of your evidence.

4 If one of the products in line for selection, as it
5 were, were DDAVP, does it maintain its effectiveness if
6 it has to be repeated in the course of a procedure, or
7 does it fall off, or what?

8 A. Thank you, sir. It has a short-term effect. And
9 usually after about 48 to 72 hours, if you are giving
10 a daily or twice daily injection, you observe
11 a phenomenon called tachyphylaxis, which is a reduced
12 response, and this is because you are trying to
13 stimulate release of the patient's own endogenous
14 Factor VIII, von Willebrand factor complex. It starts
15 with the von Willebrand factor that comes from vesicles
16 in the endothelial cells. They only have a finite
17 storage capacity. So you can flog the patient's
18 endothelial cells with DDAVP, desmopressin, and there is
19 individual variation, but usually, after four doses of
20 desmopressin, you don't get any more bang for your
21 bucks. So you have to bear in mind that limited
22 situation.

23 THE CHAIRMAN: So there is a factor particular to DDAVP that
24 might limit it as a product of choice in particular
25 circumstances?

1 A. Exactly.

2 THE CHAIRMAN: Is it also a factor that it might lead to
3 fluid build-up, especially in children?

4 A. Yes, indeed, and we were one of the first centres to
5 report that, just after Professor Mannucci in Italy
6 published in the Lancet the use of desmopressin in the
7 late 1970s. We tried in on a patient with moderate
8 severity Haemophilia A in Glasgow to cover a tooth
9 extraction, and given the recommended doses, which had
10 been worked out by the experience of about 50 or 60
11 patients in Italy, during which they had found no
12 evidence of water intoxication, fluid retention. Our
13 patient developed severe hyponatremia, the serum sodium
14 went down from 135-ish to about 110, and the patient
15 developed headaches, and that was the first clinical
16 evidence we published in a letter to the Lancet, that,
17 as you might predict from the physiology and
18 pharmacology of the situation, there are some patients
19 who are more susceptible, due to genetic factors or
20 whatever, to water retention than others.

21 So we recommended that water intoxication should be
22 always considered routinely and that particularly if
23 prolonged infusions were being given over perhaps more
24 than a day, one should monitor the serum sodium and
25 closely observe the patient.

1 Shortly after that, over the next five years,
2 several paediatric centres around the world reported
3 seizures in children, and children are more susceptible
4 to water intoxication than adults. So it is there in
5 the literature as one of the cautions to desmopressin
6 that, particularly in children, it may be toxic and that
7 should be carefully considered, fluid restriction,
8 monitoring of serum sodium, et cetera.

9 It's not the only adverse effect of desmopressin.
10 There are some patients who are intolerant to the
11 vasoactive effects, so that during the infusion, even if
12 you try to prolong that over 60 minutes, some patients
13 flush, they have a fall in blood pressure and feel so
14 uncomfortable that they say, "I don't want that
15 medication". And there are some patients in whom it is
16 ineffective, some who have the immediate intolerance,
17 some who have the delayed intolerance of water
18 intoxication. And also you are elevating the levels of
19 Factor VIII and von Willebrand factor and occasionally
20 you get thrombogenesis, so if you put the Factor VIII or
21 von Willebrand factor levels up too much, you can get
22 venous thrombosis or arterial thrombosis, which is
23 clearly undesirable.

24 So I think the point I'm making is that desmopressin
25 is not the panacea. It had a very useful place -- let's

1 not underestimate it -- during the 1980s, in sparing
2 many patients with haemophilia and von Willebrand's
3 disease around the world from getting virus infections.
4 So it has its place, but it's not the panacea. And you
5 have to assess every patient individually across the
6 whole spectrum of haemostatic agents, not only in this
7 period of time that we are talking about, concentrates
8 versus cryoprecipitate or fresh-frozen plasma, but at
9 the desmopressin end, we always tried to make sure, as
10 in all haemophilia centres, I'm sure, that any patient
11 in whom you are considering desmopressin, had to have
12 a trial dose for efficacy and safety, and then you could
13 individualise the treatment.

14 THE CHAIRMAN: Mr Anderson, I don't know whether you want to
15 follow that. I was merely trying to extend the question
16 of choice a little bit further.

17 MR ANDERSON: No, thank. I think it's helpful.

18 THE CHAIRMAN: Mr Johnston, do you have any questions?

19 MR JOHNSTON: No, I don't, sir.

20 THE CHAIRMAN: Ms Dunlop?

21 Further questions by MS DUNLOP

22 MS DUNLOP: Could I ask one more question about
23 desmopressin, please?

24 Professor Lowe, I think we have had the impression
25 that DDAVP is useful for the planned intervention, and

1 I think we can understand that, but that its role in
2 relation to the patient who needs treatment for a bleed
3 is limited to very minor bleeds, but I'm inferring from
4 what you are saying that it may also have a role in more
5 significant bleeds. Is that wrong?

6 A. It's a question of degree.

7 Q. Yes, perhaps if you can -- I don't know, think of some
8 examples and I suppose take into account what the
9 starting level of the patient's Factor VIII might be.

10 So perhaps if you can talk us through, say, the nose
11 bleed, to take one example, and then up to a more
12 significant bleed but also differentiating between the
13 person who has mild haemophilia and the person who has
14 more severe haemophilia.

15 A. Well, to take that last point first, it's only ever been
16 useful as a treatment for mild haemophilia and mild
17 von Willebrand's disease, which is, if you force me into
18 a number, 10 per cent or 10IU per DL.

19 On that basis, if you give the average patient, with
20 either of those conditions and a level of 10 per cent
21 Factor VIII, or von Willebrand factor in the case of von
22 Willebrand's disease, a standard dose of desmopressin,
23 that will elevate it two to fourfold. So you are going
24 to get up to 20 to 40 per cent of normal.

25 That, experience has shown, is usually effective for

1 preventing bleeding following dental extractions or
2 other minor types of surgery, particularly if you
3 accompany it, in the case of dental extractions, with
4 tranexamic acid, which acts by stopping the clot being
5 broken down once they have made it.

6 It has been used for treatment of established
7 bleeding, of which the most common example is somebody
8 who has had a dental extraction and then comes back
9 a few days later with secondary haemorrhage, bleeding
10 again. And you can try desmopressin in that situation.

11 Obviously, the longer it has been since that first
12 few doses of desmopressin, the more likely it is that
13 the patient's endothelial cells will have synthesised
14 more von Willebrand factor and it will work again.

15 The problem is that if you get up to between 20 and
16 40 per cent, say, in a 10 per cent patient, is that
17 enough for bleeding which has already started, as
18 compared to trying to prevent bleeding before the
19 extraction. And in general it's less effective but it
20 may still be worth a try.

21 So thinking back as to what we have done when I was
22 a practising doctor, in that situation, if somebody had
23 come back a few days after a desmopressin-treated tooth
24 extraction or other minor surgery and was bleeding
25 again, yes, we would give it a try but we would say to

1 the patient, "Let's try this and let's try all the
2 measures, but at the end of the day, if the bleeding is
3 continuing and if it's going to seriously affect your
4 health, we may have no alternative but to go to clotting
5 factor". And before recombinant Factor VIII came in,
6 that would have to be a blood product.

7 Q. What about not the patient who has had a planned
8 intervention and who comes back with more established
9 bleeding, but the patient who presents for the first
10 time with a joint bleed, say. Can it have any role
11 there? Is it worth a try there?

12 A. If such a 10 per cent patient came in rapidly after
13 a knock and you had a very early joint bleed or muscle
14 bleed, again you could give it a try but I would not be
15 optimistic. I think that patient is much more likely to
16 require clotting factor treatment.

17 Q. Right. Thank you very much, professor.

18 THE CHAIRMAN: Mr Di Rollo, there has been quite a lot of
19 discussion of DDAVP. Is there anything in that context
20 that would excite you into asking a further question?

21 MR DI ROLLO: I don't think so. I'm grateful for that
22 opportunity.

23 THE CHAIRMAN: Professor, thank you very much.

24 MS DUNLOP: Our next witness, sir, is Professor Ludlam.

25

1 PROFESSOR CHRISTOPHER LUDLAM (continued)

2 Questions by MS DUNLOP

3 THE CHAIRMAN: Good afternoon, Professor Ludlam.

4 MS DUNLOP: Thank you, sir.

5 Good afternoon Professor Ludlam.

6 A. Good afternoon, Ms Dunlop.

7 Q. We are examining, as you know, our topic C3A. We have
8 a statement from you on that topic and I should ask for
9 it to appear on the screen. It's [\[PEN0171790\]](#). We will
10 also be going to an appendix, which you have prepared to
11 be read along with this statement, and it's probably
12 just as well to open that up now too because we may need
13 to flick between them. It's [\[PEN0171798\]](#).

14 To start then with the statement, you have given us
15 a preamble and you say that:

16 "Consideration of therapeutic policy in our chosen
17 period with respect to non-A non-B Hepatitis cannot be
18 considered in isolation from the risk of other viral
19 infections, especially HIV."

20 We understand the consideration that you advance to
21 justify your statement. I wonder if it would be fair to
22 say, however, that the therapeutic policy generally over
23 this period would be guided by a desire to avoid the use
24 of blood products unless there was no alternative?

25 A. That, I think, is fair, yes.

1 Q. Right. You have, of course, also already pointed out,
2 I think in the context of our earlier topic about viral
3 inactivation in the early 1980s, that of course, the
4 whole genesis of the viral inactivation projects was
5 hepatitis, or that was the underlying risk that these
6 projects were devised to meet and that it was only
7 really as a result of the advent of AIDS that the target
8 perhaps moved slightly.

9 Question 1 we posed in relation to this period
10 between 1985 and 1987, and we asked you if there was an
11 awareness among treating haemophilia physicians in
12 Scotland that the Scottish product was less effectively
13 treated against non-A non-B Hepatitis. And your answer
14 is that:

15 "When the first heat-treated product, NY 68 degrees,
16 two hours, was introduced in December 1984, it was
17 widely acknowledged that it was very likely to transmit
18 non-A non-B Hepatitis."

19 You refer to your summary, which I think I would
20 like to go to without further ado. Can we go to the
21 other document, [\[PEN0171798\]](#).

22 You take us back to 10 December 1984, at the meeting
23 of reference centre directors, and I thought it would be
24 useful if we just looked with you at some documentation
25 about that. Could we go to something we have already

1 looked at this morning, [\[SGF0012388\]](#).

2 Just to refresh your memory. I'm sure you have
3 looked at this again recently, can we just go down to
4 the same part actually, the foot of page 2 or on to
5 page 2.

6 We have the "Options" and then the
7 "Recommendations". That's really the section that I'm
8 asking you to have in mind, and actually you have
9 reproduced this for us in your appendix so you have
10 reproduced it down to -- can we go over the page,
11 please? -- the statement that begins:

12 "In individual patients, there may need to be
13 a choice."

14 Which we can see there. And you have included up to
15 and including the words, "until all supplies are
16 heated". So approximately halfway through that
17 paragraph there.

18 Of course, that comment that:

19 "Directors may wish to continue to use unheated NHS
20 material until all the supplies are heated.

21 That really applied more to England and Wales at the
22 time this document was written in December 1984, didn't
23 it, because in Scotland all Factor VIII was being
24 heat-treated?

25 A. Yes, this refers to Haemophilia B as well.

1 Q. Well, yes.

2 A. And there was the question of Factor IX concentrate and
3 whether to use heated or unheated NHS concentrate.

4 Q. Yes. Just to look at some documents that relate to the
5 meeting itself, rather than this, which is a guidance
6 document emanating from the reference centre directors
7 a few days later, can we look firstly at [\[DHF0030898\]](#),
8 please? Can we go to the end of this, please?

9 We can see that this is from somebody within DHSS
10 who, as the author says, was invited to the meeting. So
11 that's just to give you the context of this document.
12 Can we go back then to the first page? Do you see that?

13 Paragraph 2:

14 "As you know, I was invited to the above meeting
15 held at CBLA headquarters and arranged to discuss the
16 implications of AIDS for haemophilia patients."

17 It's recorded that this guidance letter is coming,
18 and that's the document we have just looked at.

19 Then the following main issues were discussed:
20 testing patients, dealing with patients, and then on to
21 the next page, please:

22 "Use of heat-treated Factor VIII. After prolonged
23 discussion, it was agreed that children should be
24 treated with cryoprecipitate or, if necessary, with
25 heat-treated Factor VIII."

1 You and I have discussed this meeting before,
2 Professor Ludlam, and you have told us that there really
3 was a lot of discussion and debate, and I think that --

4 A. That is correct.

5 Q. -- this observer has noticed that, but I was interested
6 because this does seem to be a slightly different
7 emphasis:

8 "It was agreed that children should be treated with
9 cryoprecipitate or, if necessary, with heat-treated
10 Factor VIII."

11 Of course, I'm sure anyone would understand that
12 there would have to be a case by case assessment and
13 that individual doctors would have discretion to assess
14 the circumstances of an individual patient, but I just
15 wondered if you recall that slight preference for
16 cryoprecipitate in children.

17 A. Well, the following sentence says:

18 "New haemophiliac patients shall be treated with
19 heat-treated Factor VIII."

20 Q. Yes.

21 A. And children --

22 Q. Are often new haemophilia patients?

23 A. -- are often new diagnoses. So this isn't quite, sort
24 of, consistent. It -- what it doesn't deal with, I
25 think, is the severity of the haemophilia. Can I just

1 read it a bit further on?

2 Q. Yes, certainly. (Pause)

3 A. Yes, it opens up the debate and difficulties about
4 whether to use unheat-treated NHS product, versus
5 heat-treated commercial.

6 Q. Yes. And that, as you say, is a debate that would be
7 taking place in Scotland in relation to Factor IX.

8 A. Yes.

9 Q. Yes. But I suppose one could read the second sentence
10 as referring to patients presenting for the first time
11 but not in childhood.

12 A. It could be, yes, certainly. It's a patient not
13 previously diagnosed, found to have haemophilia and how
14 should they be treated, and with concentrate.

15 Q. Yes. Well, let's look at what I think are a more
16 official set of minutes, [\[SNF0013850\]](#).

17 I think, notwithstanding its entitlement as "notes",
18 it is really the minutes and we can see that you were
19 there and also Dr Forbes.

20 I really just want to go to page 4 but perhaps if we
21 move slowly through the first three pages, just so
22 everyone can see what was on the agenda. Screening we
23 can see. Then page 2, still tests. Page 3. Dr Tedder
24 is explaining his virologist's viewpoint, and then on to
25 page 4, please. Advice to patients and donors. Then

1 further down:

2 "Factor VIII concentrates.

3 "It was agreed that heat-treated products should be
4 given to all patients, if freely available, to include
5 those found to be antibody-positive. Antibody-negative
6 patients. It was agreed that from now on treatment must
7 be with heat-treated material."

8 No doubt subject to considerations of supply.

9 Then on to the next page, please, we can see various
10 contributions. If we can just scroll a little bit
11 further down, thank you, before we move on to advice and
12 testing of staff.

13 Can we then go on to the last page of this document,
14 please? It was just that bit that we can see at the
15 bottom of the screen. Item 6:

16 "Advisory statement. At this point Dr Lane
17 suggested that for the remainder of the meeting, the
18 haemophilia directors be allowed to have a private
19 meeting with only themselves present. This was
20 accepted."

21 So the fractionators left. Is that right?

22 A. I presume so, yes.

23 Q. Yes. Do you remember this, that the format of the
24 gathering was that there was this discussion involving
25 everybody and then people from the transfusion services

1 left. I'm not sure whether our mystery person from the
2 Department of Health stayed or went but you had
3 a private meeting, the reference centre directors had
4 a private meeting, and what, thrashed the issues around?

5 A. I think that's what happened. I think it was quite late
6 in the afternoon by the time the main meeting had come
7 to an end.

8 Q. Right. And the actual production of that advisory
9 document, was that really pulled together by
10 Professor Bloom?

11 A. Yes.

12 Q. Yes. Okay. Can we go back then to [\[PEN0171798\]](#),
13 please? On to the second page.

14 You tell us that the guidance set out in this
15 important document was adopted for treating patients in
16 Scotland.

17 The next page, please.

18 There is a reference in your paragraph 3 to what
19 happened in December:

20 "Patients were invited to return their unheated
21 stock and were given in exchange the heat-treated
22 stock."

23 I would like to come back to that, if we can
24 loosely, and I think slightly inaccurately call it,
25 "product recall". So we'll come back to product recall

1 later.

2 In paragraph 4 you are emphasising that during 1985
3 to 1987, the principal concern of those concerned with
4 haemophilia therapy was to prevent further HIV
5 transmission. You say that:

6 "Non-A non-B Hepatitis virus is seen as a much less
7 severe infection than HIV."

8 Actually, pretty much everything one can think of is
9 a much less severe infection than HIV, certainly as it
10 appeared at that time.

11 A. At that time, yes.

12 Q. Yes. And there also, you say, was an understanding that
13 it was much harder to eliminate hepatitis viruses from
14 concentrates. I wanted to suggest to you that there was
15 actually quite a lot of uncertainty about non-A non-B
16 Hepatitis at that time, perhaps not so much in relation
17 to incidence but in relation to severity. The incidence
18 seems to have been widely understood to be very, very
19 high in those treated with factor concentrates. That
20 would be correct, wouldn't it?

21 A. Unheated concentrates, yes.

22 Q. Unheated concentrates, yes. And certainly we have
23 looked in previous sessions at the work of Dr Craske in
24 UKHCDO in looking at the problem of hepatitis-associated
25 with concentrates, and we know that material started to

1 come through. We have looked at an article published in
2 1983, for example, showing a very high incidence of
3 hepatitis in people given concentrates for the first
4 time, whether NHS or commercial.

5 As far as severity, however, the picture seems to
6 have been a little less clear, and I wanted to, in
7 preparing for today, try to look at articles that might
8 have caught your eye. Jumping forward in time here to
9 [\[LIT0013859\]](#), please. We noticed it because it emanated
10 from Edinburgh, but if we look at the second page, we
11 can see that this is a letter that you and colleagues
12 sent.

13 Can we just look at the second page to see the
14 authors? Thank you. Here we are.

15 This is you sending a letter to the Lancet and it
16 was published on 2 September 1989. But what's
17 interesting about it is that it seems to show an
18 expectation on your part that really all your patients
19 might be HCV-positive had you started testing them
20 around this time. Is that correct?

21 A. The vast majority who had received pooled concentrates
22 or a great deal of cryoprecipitate.

23 Q. Yes. So can we just remind ourselves of the first part
24 of the letter. Can we go back, please, to the previous
25 page?

1 What was happening was that pretty quickly after
2 some sort of test had become available for HCV
3 antibodies, you were looking at your patient group to
4 see what the prevalence was. Is that right?

5 A. That's correct, yes.

6 Q. And you looked at this particular number of 48 patients,
7 who had received non-heat-treated products before 1985,
8 41 of them were seropositive. Then you make that
9 comment in relation to that 85 per cent figure, ie 41
10 out of 48. If we read over on to the next page:

11 "We do not know why all such patients are not
12 anti-HCV-positive."

13 You say:

14 "All would be expected to be infected."

15 We have speculated, Professor Ludlam, that there
16 might have been something to do with the kits, that the
17 sensitivity of the first generation testing kits was not
18 as good as some later kits, or an explanation of that
19 sort. But at any rate, it shows firstly a very high
20 prevalence and secondly an expectation on your part that
21 that would be so.

22 A. Yes, I think that's correct. And there always seems to
23 be the possibility there are, in fact, a few patients
24 exposed to unheat-treated concentrate who do not develop
25 Hepatitis C infection. And the reason for that I don't

1 understand. It may relate to their tissue type or
2 something rather individual in that, I think, in that
3 person.

4 Q. Yes. We understand that there are obviously genetic
5 differences between individuals, which may govern their
6 response to infection.

7 Just to look at, as I said, articles that I thought
8 maybe would have caught your eye at the time, can we
9 look firstly at [\[LIT0010335\]](#)?

10 We know that there is a companion work, which was
11 entitled "Progressive Liver Disease in Haemophilia: an
12 Overstated Problem", and that it emanated from
13 Manchester and had been published a couple of years
14 before this one, but do you remember noticing this
15 article at the time? Would this be something where you
16 would think, "I need to read that"?

17 A. Oh, yes, this was an important article.

18 Q. Right. I expect at the time you knew Dr Hay?

19 A. Indeed, yes.

20 Q. I don't think we necessarily need to go through it in
21 any detail but the general thrust of the article is
22 really betrayed by its title, that the problem may be
23 more serious than some people had appreciated. Is that
24 right?

25 A. I think it was the progressive nature of the problem

1 that perhaps hadn't been appreciated adequately, prior
2 to this paper.

3 Q. Yes. So they are saying -- and we just get this from
4 the summary -- that:

5 "Serial liver biopsies had shown progression from
6 chronic persistent hepatitis to chronic active hepatitis
7 and cirrhosis within six years, suggesting that chronic
8 persistent hepatitis in haemophiliacs is not as benign
9 as hitherto supposed. Symptoms and abnormal physical
10 signs were uncommon in these patients; in other words,
11 it may be an insidious onset."

12 A. Absolutely.

13 Q. Yes:

14 "It is anticipated that liver disease in
15 haemophiliacs will become an increasing clinical problem
16 in future."

17 Just to let you have a brief look, perhaps, at the
18 rest of it. They are reporting their observations.
19 Patients and methods. They have been screening their
20 patients since 1977. I'm sure you have told us this
21 before, Professor Ludlam, but perhaps you can remind us:
22 is that sort of screening something that formed part of
23 your regular review of your patients?

24 A. Very much so. Every few months they would have their
25 liver function tests measured, going back before my time

1 into the 1970s. And it's full of results of liver
2 function tests.

3 Q. Then they have done a percutaneous liver biopsy in 34
4 patients, and actually I think this is an article with
5 a table, or maybe I'm misremembering. Can we move
6 through it onto the next page? Yes, there is a table of
7 results at the bottom there, then the discussion:

8 "Progressive liver disease is a potentially serious
9 problem in haemophilia. Of 79 haemophilic patients,
10 selected solely on the basis of previous exposure to
11 blood products, 17 had evidence of progressive liver
12 disease ... serial liver biopsies showed progression of
13 chronic persistent hepatitis to chronic active hepatitis
14 and cirrhosis within a period of two to six years."

15 And the reference to explanations for this. The
16 widespread introduction of the treatment in the
17 mid-1970s. Then on to the next page, please, some of
18 the histology is reproduced. And then the concluding
19 paragraph is worth looking at too. They are predicting
20 that deaths attributable to liver disease in haemophilia
21 will become more common.

22 The next article I wanted to look at, the next
23 publication, is [\[LIT0010505\]](#). I'm sorry, I should have
24 recorded, that's 29 June 1985, that article.

25 So just to locate it time-wise. The next one is

1 from Blood, August 1985, and we can see that if we go on
2 to the second page of this, please. Even though you
3 were a haematologist, Professor Ludlam, I don't want to
4 take for granted that you consulted Blood. Did you see
5 this regularly?

6 A. Yes, this is one of the journals that we try and read
7 regularly.

8 Q. And will have done at the time?

9 A. Yes.

10 Q. One of your staples?

11 A. Yes.

12 Q. Right. We recognise the name of Dr Aledort. This is
13 referred to in other publications, this one. Do you
14 remember noticing this one at the time?

15 A. Yes.

16 Q. Right. And you will have read it too?

17 A. A long time ago, yes.

18 Q. Yes, and no doubt looked at it again recently?

19 A. Perhaps a year or so ago.

20 Q. Right. And in the context of the sorts of studies that
21 were being done, we can see this is quite a large study,
22 so it's talking about 155 haemophiliacs. Clinical
23 information, they say, on the frequency of complications
24 from biopsies in 115 haemophiliac patients provided
25 a unique opportunity to assess the safety of liver

1 biopsy. Then they say that the incidence of cirrhosis
2 at 15 per cent and chronic active hepatitis at
3 17 per cent was lower than previously reported. The
4 frequency of severe liver disease in patients receiving
5 large pooled concentrates was no greater than in
6 patients treated principally with cryoprecipitate or
7 plasma. They point out also the risks of liver biopsy
8 in this setting, which I think we can understand.

9 THE CHAIRMAN: Professor, what about the team? Dr Aledort
10 on this occasion seems to have quite a number of
11 supporters, as it were. What about their status? Do
12 you know any of these people?

13 A. Yes, my recollection of this paper is that they had
14 collected up these biopsies, or the slides from the
15 biopsies, from many haemophilia centres in the States.
16 This wasn't a study, I think, done at one
17 haemophilia centre.

18 MS DUNLOP: Yes, it says in the slightly smaller type, if we
19 go down to the left-hand side, sir. There is
20 a description of methodology, which explains that they
21 had a small group who were designing the study, and then
22 they say -- actually it went beyond the United States.

23 A. Yes, it was a multi-centre study and the authors at the
24 top. Dr Aledort was the director in charge of a major
25 haemophilia centre at Columbia in New York.

1 Peter Levine ran a very go-ahead
2 haemophilia centre, very concerned with blood safety, in
3 Worcester, just outside Boston, about 60 miles west of
4 Boston. Margaret Hilgartner, I think was a paediatric
5 haematologist, looking after children in New York.

6 PROFESSOR JAMES: I can do most of the rest.

7 MS DUNLOP: We should understand the team to be a mixture of
8 haemophilia clinicians and hepatologists --

9 PROFESSOR JAMES: From Bianchi onwards. Bianchi, Desmet,
10 Scheuer and Popper were all pathologists, actually,
11 respectively from Switzerland, Belgium, London and
12 New York, and Berk was a hepatologist from New York.

13 MS DUNLOP: Thank you.

14 THE CHAIRMAN: I think I could also get an answer to my
15 question about their standing from Professor James.

16 PROFESSOR JAMES: Yes, they had the highest standing in the
17 world at that time, the liver doctors.

18 A. And the same applied to the haemophilia doctors.

19 MS DUNLOP: I'm sure of that.

20 Similar sorts of descriptions of materials and
21 methods, patient classification, and the patients were
22 divided into different groups, depending on their
23 treatment history. Perhaps interesting to note that
24 there were some who had received a lifetime exposure of
25 more than 100,000 units of concentrate. Then some

1 details of how the analysis was conducted by the
2 pathologists.

3 On to the next page. The results. We are told what
4 the breakdown was as between Haemophilia A and
5 Haemophilia B. And then that little table, table 1, we
6 see the text just above that:

7 "64 per cent of all cases had trivial, mild or
8 moderate hepatitic lesions and only 7 per cent had
9 severe lesions. 15 per cent had cirrhosis and
10 14 per cent had other lesions."

11 Their -- "verdict" is perhaps the best word.
12 I don't want to say "spin" or "gloss", but if we look at
13 the discussion, which we find on page 370 of the
14 article, so two pages further on, they are highlighting
15 the fact that their finding of 15 per cent having
16 cirrhosis was less than previous reports. Actually, one
17 of the references there is to a previous Sheffield
18 paper. So in tone this is not an alarmist piece; it's
19 saying that their finding is less than some other
20 people's findings. But they do go on to say on the next
21 page that -- and this is reading the first full
22 paragraph:

23 "The lack of severity of the histopathologic
24 findings in the current materials may not be entirely
25 reassuring. Some recent evidence suggests insidious

1 progression of non-A non-B Hepatitis to cirrhosis,
2 although other studies suggest the possibility of
3 reversion toward normal hepatic architecture."

4 Then they go on to deal, towards the end, with their
5 separate findings on the risks of liver biopsy in
6 patients with haemophilia.

7 I'm saying "separate" but, of course, it's not an
8 entirely discrete consideration because I think we can
9 understand that if a clinician wants to try to assess
10 the condition of the patient's liver, he or she is going
11 to want to do a biopsy and for patients with haemophilia
12 that raises particular problems. So not surprising that
13 they are also devoting part of their study to that
14 particular topic.

15 A. Very important that they do so, yes.

16 Q. Yes. The other publication -- it's actually a letter --
17 I wondered if you might have noticed at the time is from
18 the Lancet of February 8th 1986. The reference for it
19 is [\[LIT0010341\]](#) but on the next page. We can see there
20 a letter from a Dr Schimpf. Another well-known name?

21 A. A very well-known name. A very distinguished
22 haemophilia treater.

23 Q. Yes. Liver disease in haemophilia. And he -- yes? He
24 is a he?

25 A. He is a he, yes.

1 Q. He is aligning him with Hay and others, the Sheffield
2 authors. He says:

3 "Like Hay et al, we think that progressive liver
4 disease is an understated problem."

5 And he is offering his own figures from his centre.
6 They found progressive liver disease in 29 per cent of
7 their patients, 16 per cent having chronic active
8 hepatitis and 13 per cent having cirrhosis. "He
9 multi-centre study by Aledort et al, to which he
10 contributed biopsy material, came to a similar
11 conclusion about the frequency of cirrhosis."

12 So perhaps interesting just to maybe gently contrast
13 the tone. I don't know if this is my imagination as
14 a layperson but if the tone of the Aledort piece is that
15 the frequency of serious liver disease is not as high as
16 others are saying, whereas this, taking very similar
17 sorts of figures, is saying that it is an understated
18 problem, it seems to be giving perhaps a slightly
19 different sort of spin or gloss to very similar data.
20 Is that reasonable or am I off line?

21 A. No, I think it's reasonable and I think the crucial
22 thing is whether it is progressive.

23 Q. Right.

24 A. Because one might say 13 per cent cirrhosis is one thing
25 and might be seen as not a severe problem, but if the

1 liver disease is progressive, so you go back five years
2 later and, instead of it being 13 per cent, it's
3 25 per cent, then it's serious.

4 Q. Yes.

5 A. But there was, as you know, a debate from mid/late 70s
6 onwards as to how progressive, how severe, liver disease
7 was but I think around about this period was when it
8 became clear that it was potentially serious and
9 potentially progressive.

10 Q. I'm obliged, Professor Ludlam, because you are really,
11 I think, focusing for us something that I certainly
12 hadn't completely appreciated and that is the need to
13 take on board the use of the word "progressive". That
14 is the title of the Sheffield paper, "Progressive Liver
15 Disease in Haemophilia". So it's not just liver disease
16 in haemophilia, it's progressive liver disease that
17 people are worrying about?

18 A. That's as I see it, yes.

19 Q. Yes. Do you remember noticing this letter?

20 A. I'm sure I saw it.

21 Q. Yes. Can we go back then, please, to where we were,
22 which is in the appendix, [\[PEN0171798\]](#). We were on the
23 third page of that, so at 1800. I did put to
24 Professor Thomas, when he was here earlier this week
25 talking about this problem, the proposition that in an

1 era where the data was a bit uncertain much depends on
2 the question one posed. So if the question had been,
3 "Are we dealing with a very serious problem," it might
4 have been difficult to give it a very meaningful answer,
5 but if the question had been, "Is this something we
6 don't have to worry about," the answer to that would be
7 that one couldn't be reassured; it was something to be
8 concerned about. Is that reasonable?

9 A. Sorry, is this in relation to the two-hour heat
10 treatment?

11 Q. No, no, liver disease in haemophilia, progressive liver
12 disease in haemophilia. It might have been difficult to
13 get an absolute sense of the magnitude of the problem.
14 But, equally, at the other end of the spectrum, as it
15 were, one wouldn't be saying, "This is something that
16 needn't concern me."

17 A. Oh, yes, I agree.

18 Q. Right.

19 A. I'm sorry.

20 Q. No, it's my fault.

21 You make the point in paragraph 5 that there were
22 studies from 1985 onwards which were showing both
23 continued transmission of HIV and continued transmission
24 of non-A non-B Hepatitis by heat-treated or otherwise
25 treated concentrates. I think we know that to be true

1 and I don't think we need to go to those documents in
2 relation to HIV. We know there was a problem with
3 Armour heat-treated concentrate, and the second of those
4 references is an article we have looked at many times
5 already by Kasper in the transfusion periodical, I think
6 in 1993.

7 Then you say in paragraph 6 that:

8 "When the first heat-treated product was introduced
9 in Scotland, it was uncertain whether it would transmit
10 HIV and to what extent, if any, there was a reduced risk
11 of non-A non-B Hepatitis."

12 Then you talk about evidence about there having been
13 contaminated pools but fortunately no development of HIV
14 in the recipients of some of those pools which were
15 looked at retrospectively, and I think that reference is
16 to an article in Vox Sanguinis. Is that right?

17 A. Yes.

18 Q. For anyone who wants to look at it, it's [\[LIT0010664\]](#)
19 but I'm not proposing to go to it.

20 In section 7 you talk about the need to try to
21 assess the efficacy of heat treatment. I think we
22 understand that that could be done with HIV using the
23 virus itself because, obviously, once the virus had been
24 found, one could do experiments to see if it was
25 inactivated by a particular heat treatment protocol. It

1 was very much more difficult for non-A non-B Hepatitis
2 and I think we can understand this because we are
3 talking about a time before the virus has been
4 identified.

5 You say that there was an internationally agreed
6 protocol for that sort of work, so those sort of
7 experiments were governed by a protocol, and then you go
8 on to identify further difficulties in trying to assess
9 the hepatitis-related safety of heat-treated
10 concentrates.

11 You say it was difficult to know which previously
12 treated patients were not already infected:

13 "The ideal patient group was, therefore, those who
14 had never received a transfusion of blood or a blood
15 product and required treatment with one. It is
16 considered possible also to include patients who had
17 only been minimally exposed."

18 You say:

19 "As between these two groups, the former patients
20 only rarely present and the latter were a rather
21 heterogeneous group of individuals."

22 We understand that it was not a straightforward
23 matter to assess the safety of a product. Can we then
24 go on to paragraph 8, please, on the next page? You
25 talk about early 1985 at BPL and you say that:

1 "The initial batches of 8Y were available for use in
2 patients but it was not until October 1985 that 8Y at
3 80 degrees for 72 hours was in full production."

4 And you say that:

5 "That product only represented about one third of
6 Factor VIII concentrate used in England. The other
7 two thirds were of commercial origin."

8 But, of course, professor, in the discussion we are
9 having we should bear in mind that the particular group
10 of patients on whom you were, I think, trying to focus
11 is the previously untreated or minimally treated
12 patients. So it's not the patients who have had years
13 of concentrate therapy already who are your main
14 concern. Is that right?

15 A. Yes, and for assessing new concentrates you needed to
16 have patients who had not previously been transfused.

17 Q. Yes.

18 A. But in this paragraph 8 perhaps what I don't say is that
19 BPL went on manufacturing, as I understand it,
20 non-heat-treated NHS Factor VIII up until the spring for
21 distribution in England. In parallel they were doing
22 this development work on 8Y, so they could give some
23 test infusions and check that it was reasonable to give
24 to people.

25 Q. Right. In any assessment, however, of how well

1 a country did in meeting different needs over this
2 period, it's perhaps less relevant to look at how much
3 of the total requirement for concentrate was met by NHS
4 product, in that, when you are trying to protect
5 patients from hepatitis, the patients you are trying to
6 protect are those who you think won't already have been
7 exposed. So they are a much smaller group. Presumably,
8 the efforts of clinicians are particularly focused on
9 trying to protect those who have not already been
10 exposed?

11 A. But during this period the principal objective was to
12 avoid HIV transmission in early 1985.

13 Q. Yes. Can we go back to your statement, where the
14 position in England is dealt with in slightly more
15 detail, please? So that's going back to [\[PEN0171790\]](#) at
16 paragraph 2. This deals a little bit with what I'm
17 calling "product recall". Then paragraph 3. You say:

18 "The viral safety of this BPL product ..."

19 I think it's 8Y. We can call it that:

20 "... introduced in England in September 1985, was
21 unknown at that time."

22 That may be strictly correct, professor, but was
23 there not a kind of expectation that it would be safer
24 in relation to blood-borne viruses than products treated
25 with a lesser heating protocol?

1 A. I think that was a reasonable expectation but the
2 history of heat-treating Factor VIII concentrates to try
3 and destroy non-A non-B Hepatitis was not good, even
4 heating up to 68 degrees. Clearly, going a little
5 higher might destroy the virus or viruses but there was
6 no certainty at all that 80 degrees would be effective
7 and there was a lot of international scepticism about
8 dry heat treatment at all at any temperature as being
9 effective. If I recall correctly, the FDA was very
10 sceptical about dry heat treatment, even at 80 degrees.

11 Q. Yes. You do go on to cover that. You talk about the
12 response of the FDA. But I suppose, as the first
13 building block in trying to recreate the atmosphere of
14 the time, I was suggesting that, as soon as you heard
15 about this, whenever you did, this product in England,
16 you might be thinking, "Oh, that might be safe against
17 hepatitis as well as against HIV."

18 A. Safer.

19 Q. Safer?

20 A. Safer, rather than safe.

21 Q. Now, just to look at that question of state of
22 knowledge, can we look firstly please at [\[SNB0075664\]](#)?
23 We can see that this is a meeting that took place at PFC
24 on 17 March 1986 and some very familiar names are there
25 representing SNBTS: Dr Perry, Dr Foster,

1 Dr Cuthbertson, and I think we also have heard of
2 Dr Prowse and Dr Dawes and Dr Urbaniak, and I think
3 Mr McQuillan as well, and then some the names from BPL:
4 Dr Lane, Dr Snape, Dr Smith.

5 Can we just look through this at the topics that
6 were being discussed: This, kind of, state of play,
7 plasmapheresis. Then on, please, to the next page.
8 Dr Cuthbertson is talking about his recent model virus
9 studies. Then on to the next page, please. Do you see
10 paragraph 5:

11 "Dr Smith outlined clinical trial results of the 8Y
12 F8 product so far. While results cannot be considered
13 conclusive at this stage, he indicated that no cases of
14 virus infection have occurred attributable to 8Y
15 material after 12 months' experience of 8Y in virgin
16 haemophiliacs."

17 So, in response to your suggestion that it wasn't
18 until mid-1986 that evidence started to be reported to
19 suggest that it might be a hepatitis-reduced
20 concentrate, it looks as though there was a bit of
21 evidence before that.

22 A. It doesn't say how many patients, and we know that from
23 this study not all the patients were not previously
24 treated patients and also that the frequency of liver
25 function testing met international standards; in other

1 words, once a fortnight testing.

2 Q. All right, perhaps we could agree that it is evidence
3 and the question of the weight it should bear might
4 depend on some of the factors that you have mentioned?

5 A. Yes.

6 Q. All right, okay.

7 I wonder, sir, it's 1 o'clock. Perhaps we can
8 pursue this after lunch.

9 THE CHAIRMAN: Yes. Not immediately.

10 Professor, would you look back just for a moment at
11 [\[LIT0010335\]](#), please? I didn't want to disturb
12 Ms Dunlop's flow of thought but I do want you to think
13 about this. I think it's on the next page, the passage
14 that I'm interested in. Could you go to the next page,
15 please, and we will see? No. It's the passage that
16 refers to observation of raised ALT in the 1970s. Yes,
17 80s:

18 "The prevalence of abnormal liver function tests in
19 haemophiliacs increase rapidly with the widespread
20 introduction of Factor VIII and IX concentrates in the
21 mid 1970s."

22 Professor, what I'm interested in is whether there
23 were recorded increased levels of ALT and AST, or
24 whatever, before that in two areas: One, your area,
25 Southeast of Scotland, and the other, the Oxford area,

1 "The viral safety, with respect to the transmission
2 of non-A non-B Hepatitis, of the BPL severely heated
3 product, was unknown."

4 You point to the fact that it only met the needs of
5 about one third of the total use of Factor VIII in
6 England and go on to say that during the
7 period December 1984 to June 1986, there was no clotting
8 factor concentrate available in Scotland or anywhere
9 else in the UK which was reported and accepted to be
10 hepatitis-safe. It was necessary to assume that all
11 concentrates could transmit the causative agent, or
12 agents, for non-A non-B Hepatitis. And after June 86 it
13 was assumed 8Y was less likely to transmit non-A non-B
14 viruses.

15 Then if we go to the appendix, [\[PEN0171798\]](#), at
16 1802, I think in particular we are looking at
17 paragraph 9, so if we could go a little bit further
18 down, we can see some more details surrounding your
19 suggestion that it was really June 1986 that was
20 a turning point in the realisation that this product
21 might be safer.

22 I just wanted to look at one or two sources of
23 information over this period. Could we look, please, at
24 [\[DHF0017386\]](#)? That's a meeting of the Central Blood
25 Laboratories Authority, central committee for research

1 and development in blood transfusion. It's obviously
2 a body relating to England and Wales, taking place on
3 9 July 1985, and there is a reference to product in
4 development in this.

5 Can we go on to the page after the next page?

6 If we go down the page, please:

7 "The immediate safety and efficacy of the 8Y
8 concentrate have been demonstrated by clinical trial.
9 Eight patients at three haemophilia centres receiving 14
10 infusions of three batches of concentrate have shown
11 dose responses ..."

12 Certain figures, which Professor Lowe told us, meant
13 that the product was acceptable in doing what you would
14 want it to do from a therapeutic perspective. Then
15 evidence for a reduction or elimination of viral
16 transmission is being sought:

17 " ... after infusions in haemophiliacs who have been
18 treated with concentrate, either for the first time or
19 after a long interval, and who are thought to
20 be susceptible to infection with Hepatitis B, NANBH and
21 HTLV-III. This trial is at a critical stage but several
22 patients have already safely passed the point at which
23 the first evidence of NANBH transmission would have been
24 expected."

25 A document, which I think really goes with the

1 minutes of that meeting, is [\[DHF0030476\]](#). We looked at
2 it with Professor Lowe. This is really, I think,
3 a product information sheet from July 1985, issued by
4 BPL and dated 24 July 1985. It's going to haemophilia
5 directors in England and Wales. It's the same
6 information: it has information about the heating, about
7 the product and its performance and then a little bit
8 further down about the clinical trials.

9 So there were already some optimistic indicators in
10 the summer of 1985. I don't suggest for a minute that
11 you were at the CBLA meeting -- I'm sure you weren't --
12 but you must have been hearing news from England, were
13 you not?

14 A. I knew the studies were going on and I know that it is
15 incredibly difficult to find true, previously
16 untransfused patients and that these studies are very
17 difficult to do because of that and because you have to
18 get fortnightly samples and that often these turn out to
19 be small children, and it's difficult for all sorts of
20 reasons to get samples from small children.

21 I don't think -- I hadn't seen this last sheet that
22 has disappeared from the screen. It was distributed to
23 haemophilia directors in England and Wales. So I didn't
24 receive that.

25 Q. I accept that, professor, but I think we have been

1 painting for ourselves a picture of the haemophilia
2 doctors in Britain all being in close touch with one
3 another, being professional colleagues who did share
4 information, and it just struck me that perhaps this
5 would have been mentioned to you at a meeting or in some
6 conversation you might have had with a haemophilia
7 director in England. Did nobody say to you in 1985 that
8 the initial information coming through about 8Y was
9 looking good?

10 A. I'm sorry, it's 25 years ago. These things evolve on
11 the grapevine, if you like, informally. You sit next to
12 someone at a meeting or you have a cup of coffee with
13 them and they say, "I have had a patient who hasn't had
14 an ALT rise after they got 8Y. It's beginning to look
15 a bit promising." But exactly when I had these
16 conversations, I'm sorry, I can't remember.

17 There was a general feeling. I put it at 1986 --
18 yes, 1986. And I suppose there was a certain amount of
19 scepticism as I was hinting before lunch, about dry heat
20 treatment and its efficacy. There had been so many
21 disappointments with commercial dry heat-treated
22 concentrate apparently killing non-A non-B viruses when
23 tested in chimpanzees, but then we know, as you know,
24 that it still transmitted.

25 Q. Yes.

1 A. So there was a lot of scepticism about, as I say, how
2 effective dry heat treatments would be, however hot.
3 This difficulty was really exemplified by the
4 discussions that SNBTS were having, as to whether to go
5 for a pasteurised product, wet heating, in a liquid
6 state or whether or not to go for dry heating, and it
7 was a bit of a knife-edge decision which way to go.

8 So some of us would want quite a lot of convincing
9 that dry heat treatment really was going to be effective
10 against this or these viruses.

11 Q. I certainly take your point, Professor Ludlam, that it
12 must be near impossible to remember a conversation you
13 might have had over a cup of coffee at a meeting with an
14 English haemophilia director in 1985.

15 If we move into Scotland, however, we can see that
16 Dr Perry mentioned these developments in a report he
17 wrote in January 1986. Can we look, please, at
18 [\[SNB0015469\]](#)?

19 Dr Perry is preparing this report for what I think
20 you call the "joint meetings". I think we call them the
21 "joint meetings" now as well, the haemophilia directors
22 and SNBTS directors' joint meetings. This seems to be
23 one that's coming up in March 1986, and the report has
24 actually been written in January 1986 and he is talking
25 about supply and demand, but he does go on to mention

1 developments in England, I think in section 3, if we can
2 go forward to that, please:

3 "Heat treatment of coagulation factor concentrates."

4 A little summary of what has happened in Scotland
5 and then that paragraph that you can see towards the
6 bottom of the screen about awarenesses of what's going
7 on at BPL.

8 Curiously, professor, you don't seem to have been at
9 the joint meeting in March 1986. I think you are at
10 every other one we have ever looked at but I don't think
11 you were at that one. What would be the procedure?
12 Would you have received the background papers even if
13 you weren't going to be able to be there?

14 A. My recollection is I had sent my apologies some time in
15 advance. I think the date of the meeting had been
16 changed and I was disappointed that I wasn't going to be
17 able to attend the revised time. So I wrote expressing
18 my disappointment and I may not have received the papers
19 because I wasn't going to be there.

20 Q. I see. It's information to the same effect really as
21 the information we have been looking at in 1985 from
22 English sources, except this is coming from Dr Perry and
23 being disseminated to those attending the joint meeting.
24 Just to look at the minutes of the joint meeting, it is,
25 I think, 5 March 1986, [\[SNB0015448\]](#).

1 A. Would this not be commented -- Dr Perry not be
2 commenting in this way as a justification for --
3 Q. For the Scottish plan.
4 A. -- for the Z8 being treated at 80 degrees?
5 Q. That's how it reads, yes. It reads as a piece of
6 information that has been given in the course of
7 description of plans in Scotland.
8 A. Yes.
9 Q. Yes, but nonetheless, it's a statement in its own right.
10 It's a statement of the current position and there we
11 see the list of attendees. Are you shown in the
12 apologies? Can we go down, please? Yes, there we are.
13 So, as you said, you have sent your apologies.
14 I don't think there is any mention in the minutes of
15 the meeting of this information from England. In fact
16 there is not much point in asking you about a meeting
17 you didn't attend. So the statement seems to have been
18 contained in the background papers, and I think you are
19 telling us you are not sure whether you had the
20 background papers or not. I think you are suggesting
21 you didn't?
22 A. I may well not have.
23 Q. Yes. Can we go back then, please, to its appendix
24 document, [\[PEN0171798\]](#). We were looking at paragraph 9,
25 which is on 1802.

1 You actually identified some other sources of
2 information, which I think had actually encouraged you
3 to think in terms of it being in June 1986, that you
4 began to be aware of the apparent success of the English
5 product. You say that some preliminary evidence emerged
6 at a World Federation of Haemophilia conference in Milan
7 in June 1986. Did you attend that?

8 A. No, I took this from the preliminary report.

9 Q. I see.

10 A. And I couldn't actually see in my electronic version of
11 the preliminary report, the report referred to of the --
12 Jim Smith's paper -- it wasn't Jim Smith, it was -- I'm
13 sorry -- someone else, who I think presented it --

14 Q. We are not going to be confusing each other, professor,
15 because what I have been looking at is Dr Jim Smith's
16 paper.

17 A. In Milan?

18 Q. Yes. Can we look at that? That's [\[SNB0075955\]](#).

19 I think in our preliminary report we quote this as
20 being the source of information about proceedings in
21 Milan?

22 A. Yes, you do. I just couldn't --

23 Q. You couldn't access it?

24 A. I couldn't access it on my electronic version.

25 Q. Right. I think we suggest that what must have happened,

1 and we are obviously just speculating but nonetheless,
2 Dr Smith had prepared these notes of the different
3 presentations at the conference and had shared them with
4 colleagues in Scotland, who had perhaps not been there.

5 It does seem to me, having gone through this -- and
6 I don't want to take up time doing so now -- that there
7 isn't actually any paper referred to in Dr Smith's
8 synopsis which covered the topic of progress in England.
9 So perhaps a little bit of a conundrum. I was trying
10 get at what you were meaning when you say in your
11 statement that:

12 "Preliminary evidence emerged in June 1986 at
13 a World Federation of Haemophilia conference in Milan."

14 That's why I was looking for a mention of it in this
15 report of the conference, and I couldn't find it
16 mentioned there.

17 A. I should have given my reference as the Inquiry's
18 preliminary report, and when I clicked on the link,
19 I got this description of everyone else's studies but
20 not what the 8Y study was, so I was at a bit of a
21 loss --

22 Q. Touche, Professor Ludlam. I think we understand the
23 point you make; we will perhaps research that a little
24 bit further.

25 The other reference you give is to a paper presented

1 to UKHCDO in September 1986, and the reference for
2 that -- actually, sorry, before we leave this, could we
3 just look at page 7 of this document? I didn't want to
4 leave this document without pointing out that there is
5 a reference in it to the Sheffield work. So since we
6 are talking about liver disease, progressive liver
7 disease in patients with haemophilia, I thought it was
8 interesting to see that that was the agenda in Milan and
9 we can see that there on page 7. It's the second entry.

10 Described here, whatever the paper was, it was
11 somebody repeating the view of the Sheffield workers
12 that biopsies were revealing an alarming level of
13 progressive liver disease in haemophiliacs related
14 probably to NANBH.

15 I'm sorry, I just wanted to note that before we left
16 Milan. The reference to Dr Smith's paper is
17 [\[SNF0011123\]](#). Yes, I think this is the interim report
18 you had in mind. Is that right?

19 A. That is correct, yes.

20 Q. Yes. We can see that this report lists those providing
21 data and then it's shown that the data has been
22 summarised on 30 September 1986 by Dr Jim Smith.

23 Then can we go over, please, to the text?

24 The introduction tells us what has led to the study,
25 that there has been a protocol circulated and that

1 certain selection criteria have been applied to the
2 patients. The frequency of testing is explained,
3 products tested and then results.

4 I'll just let you read to the end of the results
5 section. (Pause)

6 Can we just look at the little bit on the next page,
7 please?

8 So, professor, you have mentioned this in your
9 written answer, and this looks to have been more
10 definitive information about the English product. Is
11 that right?

12 A. I'm not sure that this is the report that was presented
13 at UKHCDO meeting.

14 Q. All right.

15 A. This is dated 30 September.

16 Q. Yes.

17 A. And I think the UKHCDO meeting was a few days before
18 that. I suspect this is a revision and it may well be
19 the first draft of the paper that was eventually
20 published in, I think, the Lancet, in 1988, to which
21 I think there was additional patients -- we haven't got
22 to the bit that says how many patients there are in this
23 study. There were 32 in the 1988 --

24 Q. Right. Perhaps the next page has a table. There are
25 two tables.

1 Can we go on to the next page? Thank you.

2 About 15 patients maybe? 16. Yes, 16 patients. So
3 fewer patients than were eventually written up.

4 Then the final --

5 A. I mean, there are problems with this data. Patient 8Y5
6 had previously had cryoprecipitate, had an ALT level of
7 107. That is raised. I don't know whether it's two and
8 a half times the upper limit of normal. The upper limit
9 of normal might have been 40. So this is, I think,
10 probably above two and a half times. It's -- one of the
11 problems with this study is that there weren't strict
12 fortnightly samples and there were sometimes long gaps
13 after a high level with no other sample to corroborate
14 it.

15 This is a patient who has been treated with cryo in
16 the past. It could have been from the cryoprecipitate,
17 it could have been from the 8Y. Another patient, 8Y/10,
18 a few lines further down -- I'm sorry, I don't know
19 what -- an AST of 66 -- I can't remember what the normal
20 range for an AST is.

21 PROFESSOR JAMES: The same.

22 A. The same. So up to 40, so that's raised. Pre-exposure
23 suggests another patient who is probably infected,
24 either with Hep C from the cryoprecipitate, 35 packs, or
25 has some other cause for liver disease.

1 MS DUNLOP: Right.

2 A. Then at the bottom there is a 9A patient with an ALT
3 level of 102, without previous exposure, apparently, to
4 a blood product. So one wonders why that patient has
5 got a raised ALT.

6 THE CHAIRMAN: He is only five. It can't have been alcohol.

7 A. One presumes it wasn't.

8 THE CHAIRMAN: Certainly not self-administered.

9 A. There are all sorts of other causes apart from alcohol,
10 particularly in children with febrile illnesses. This
11 is interesting data, it is reassuring, but as Dr Kernoff
12 said at the meeting at which this was presented, the
13 minutes record, he says it was "soft" data. And even
14 the 1988 paper was soft data, all 32 patients of it.
15 That's why they started on a very thorough, proper study
16 to conform to the 1987 guidelines.

17 MS DUNLOP: It looks as though possibly some patients were
18 being included in the study who, in retrospect, had
19 confounding factors attaching to them, or may have had.

20 A. Or non-A non-B Hepatitis was being transmitted by 9A.

21 Q. Well, I take your point, professor, that it's not
22 perfect data -- or it's soft data, to use Dr Kernoff's
23 words -- but I think we have also been told that it can
24 be very difficult to recruit patients for a study such
25 as this. So sometimes maybe the criteria were slightly

1 relaxed with consequent diminution in the usefulness of
2 the some of the results.

3 A. That for the first study, yes.

4 Sorry, could I just say that this was in an
5 atmosphere where there was a lot of scepticism about dry
6 heat treatment. So I think it was very important the
7 results were looked at very critically, and if dry heat
8 treatment was going to be an effective way of destroying
9 the virus, then it had to be proven very clearly, not
10 just for the UK but internationally, for haemophilia
11 care throughout the world.

12 Q. Can we go back then, to the appendix document, please?

13 We were on page 5 of [\[PEN0171798\]](#).

14 You and I between us have been trying to paint
15 a picture of information available and reactions to it
16 in 1985 and 1986. You go on to tell us in paragraph 10
17 that:

18 "Immediately it was reported that 8Y may be
19 a 'hepatitis' reduced concentrate, [you] requested, in
20 July 1986, that a small stock should be available which
21 could be used for treatment of virus naive patients in
22 Scotland."

23 I think it would be helpful if we looked in a little
24 more detail at what happened in Scotland in the summer
25 of 1986, surrounding that acquisition of 8Y. Can we

1 look then, please, at [\[SNB0075869\]](#)? This is a letter
2 from Dr Boulton to Dr Cash dated 1986, and you are
3 mentioned in it. It concerns trials of Factor VIII
4 products and clearly Dr Boulton is thinking of trials in
5 Scotland; that's why he has been discussing matters with
6 you.

7 The second paragraph is interesting. Dr Boulton
8 tells Dr Cash:

9 "Apparently a few weeks ago he [that's you] was
10 asking Brian McClelland if 8Y could be made available in
11 the event of a 'virgin' haemophiliac being present. He
12 tells me that he would be happy to treat such patients
13 with a product prepared by the SNBTS that has been
14 subjected to an 'equivalent' heat treatment regime."

15 Do you remember having a first conversation with
16 Dr McClelland about this, about maybe trying to get some
17 8Y?

18 A. I think this is when there was the first discussion and
19 I'm not so sure that -- it may not have been someone in
20 blood transfusion who had passed on the latest
21 information about 8Y that had been presented at that
22 central blood transfusion safety meeting back in March,
23 that you showed me.

24 Q. Yes, well, I suppose someone who had seen Dr Perry's
25 report perhaps, that went to the joint meeting in March,

1 maybe. We are just speculating but it would make sense
2 if it was something of that nature?

3 A. I think probably I had discussed with Dr McClelland the
4 issue of the then current SNBTS product causing non-A
5 non-B Hepatitis in patients, and it had come up in
6 conversation that, you know, maybe 8Y was a better
7 product from that point of view.

8 Q. Right. Even the information in September 1986, you are
9 telling us, was soft. So information here that you have
10 in your mind must be pretty soft, but you are still
11 interested in getting some.

12 A. Yes.

13 Q. Because?

14 A. Because the evidence from the 8Y studies was that it
15 appeared to be less likely to transmit non-A non-B
16 Hepatitis, whereas it was highly likely that all bottles
17 of SNBTS, then available concentrate, 68 degrees for
18 24 hours, was likely to transmit hepatitis. So it's
19 a matter of degree.

20 Q. Yes. So it would be an improvement on what you
21 currently had?

22 A. Yes, it might not be hepatitis-free but it might be
23 less.

24 Q. Can we look at another letter, please? I think it's the
25 same date, [\[SNB0075871\]](#).

1 This is Dr Boulton to Dr Perry. It is indeed
2 27 June 1986 and again, the letter features you. It
3 mentions two patients, a virgin patient with
4 Christmas Disease who received heat-treated Factor IX
5 towards the end of 1985, who was continuing to show no
6 elevation of ALT levels or other evidence of non-A non-B
7 Hepatitis; and that Factor IX would be 80 degrees,
8 72 hours --

9 A. That's correct.

10 Q. -- heat-treated?

11 A. Right, from August -- available from August 1985.

12 Q. Right. So interesting for Dr Perry to know that.

13 A. Yes.

14 Q. And then in the second paragraph, that:

15 "A young haemophiliac who previously had minimal
16 therapy with Factor VIII received an infusion of the
17 current heat-treated product a month ago. He now shows
18 signs of liver enzyme rises indicating non-A non-B
19 Hepatitis. Christopher is a bit ruthless with his own
20 staff about this because he feels that this patient
21 should have received 8Y or an equivalent product.
22 However, the patient is apparently quite well
23 clinically."

24 Professor Ludlam, one of the things which has struck
25 us about the letter is the use of the unusual word.

1 It's perhaps not in everyone's lexicon. Were you
2 ruthful?

3 A. I was a bit sad that we didn't have 8Y to give to the
4 patient.

5 Q. Right. So you are not disagreeing with Dr Boulton's
6 characterising of your feelings on the matter?

7 A. No.

8 Q. Right. Can we look next, please, at [\[SNB0075909\]](#)? This
9 is Dr Perry writing to Dr Boulton and thanking
10 Dr Boulton for passing on your comments about
11 Factor VIII, and Dr Perry is, obviously, focusing on the
12 developments in Scotland and what he is anticipating
13 might happen:

14 "Scotland is poised to introduce yet another
15 Factor VIII product, which will be heat-treated at
16 80 degrees for 72 hours and should therefore be
17 comparable to 8Y and better than anything available
18 commercially."

19 And Dr Perry is anticipating that:

20 "As soon as this becomes available, virgin patients
21 will be able to gain access to this product before
22 stocks of the existing product are exhausted."

23 The next letter we need to look at is the next in
24 number, [\[SNB0075910\]](#). This is still on the same topic,
25 that is what is to be expected in Scotland over the next

1 few months.

2 THE CHAIRMAN: Have we got the right letter?

3 MS DUNLOP: Yes, it's Dr Boulton back to Dr Perry and it's
4 enclosing notes of a telephone conversation, which we do
5 also have but it's handwritten, and in our preliminary
6 report we have reproduced it in typewritten form.

7 So I was going to look at that because it's easier
8 to read, and that's [\[LIT0012718\]](#) at page 82. There it
9 is. In the hard copy it's page 506. Can we just look
10 at that table, please?

11 So Dr Boulton wrote to Dr Perry with manuscript data
12 thought to reflect a telephone conversation between them
13 on future production, and we can see that Dr Boulton has
14 sketched the whole thing out, you know, what is to be
15 looked forward to by way of new production in Scotland.

16 Interestingly for our purposes, on the bottom
17 right-hand corner of the table is a statement that from
18 about September 1987, the PFC version of 8Y will be
19 produced:

20 "Hence half-life and recovery studies + NANB
21 et cetera on 'virgin' haemophiliacs are required."

22 Then a line along the bottom:

23 "In the meantime, any Edinburgh virgin haemophiliacs
24 requiring therapy could be given BPL 8Y."

25 So the idea is definitely circulating at this time

1 of trying to obtain a stock of 8Y for a particular
2 category of patients, if we can put it like that for the
3 moment.

4 A. But it was also the plan that there would be
5 an 80-degree, 72-hour product starting to be produced
6 in September 1986.

7 Q. Yes.

8 A. So not waiting until the box in the bottom right-hand
9 corner --

10 Q. Yes, indeed, I take your point that there is
11 a difference between when there might be some available
12 for certain patients and when it is the product
13 available generally?

14 A. No, I think the bottom right-hand box is a phase 4
15 product. That is a new formulation of Factor VIII, what
16 they described, I think, as "phase 4" in the original
17 diagram.

18 Q. Right.

19 A. The phase 3, the one that starts in September, I think
20 was Z8.

21 Q. Right.

22 A. Okay? I think the one on the bottom right-hand corner
23 was going to be a higher purity, new product, completely
24 different.

25 Q. Right. Let's look at the handwritten version,

1 [\[SNB0075911\]](#).

2 A. At the bottom of this screen -- oh, sorry.

3 Q. There we are. It doesn't actually mention a phase 4 but
4 that's your recollection --

5 A. On the previous screen, just below the diagram, there
6 was some text that mentioned a phase 4.

7 Q. Right.

8 A. If I can go back to that.

9 Q. Okay. Can we go next to [\[SNB0075913\]](#), please? There we
10 are.

11 This is Dr Perry to Dr Boulton on 7 July 1986. The
12 heading is "Factor VIII trials", and Dr Perry appears to
13 be thanking Dr Boulton for the handwritten table. He
14 goes on to make a couple of comments about the phase 4
15 product, as you pointed out. The manufacturer can't
16 resist adding that the product is more than equivalent
17 to 8Y; it's much better. But in the second paragraph,
18 Dr Perry turns his attention to the needs of the moment.
19 He says:

20 "While there will be no PFC product virucidally
21 comparable to 8Y until September 1986, after that time
22 it would be my intention to supply the phase III product
23 to 'virgins' since we hope to demonstrate by that time
24 that it is virucidally equivalent thus removing the need
25 to go South. However, in the immediate future

1 (July-September 1986), we could probably get supplies of
2 8Y for special cases. It would of course be preferable
3 if these were obtained and supplied through PFC."

4 Just seeing what happened about that, the next
5 letter is [\[SNB0075914\]](#). This is Dr Boulton again. He
6 is writing Dr Perry on 7 July 1986, and now the focus is
7 actually on the interval before some Scottish product is
8 available.

9 Dr Ludlam has written to Dr McClelland asking if it
10 will be possible to obtain some of the BPL products.
11 This is for use if a previously untreated haemophilic
12 presented for replacement therapy. Difficult to
13 estimate his potential use accurately.

14 I should say we have looked for this letter but
15 I don't think we have it, but we get the general gist of
16 it from this one, as it were. We have looked for that
17 letter, I should say, to make it clear.

18 Dr Boulton has some reservations about the sorts of
19 quantities which could be requested and perhaps granted
20 from BPL. There is a bit of debate about that.

21 Dr Boulton is wondering if Dr Perry can get perhaps
22 50 vials. And his thinking on that is that:

23 "50 vials would at least enable us to cover the
24 initial injection for such a case, and if the need were
25 to arise to call up more from Oxford over the course of

1 24 hours or so."

2 And [\[SNB0075980\]](#), please, which is now the
3 involvement of BPL to Dr Perry on 24 July 1986. The BPL
4 response has been that they are willing to supply 8Y but
5 they would like also to get some information about any
6 data that you obtain by using it.

7 A. That's correct, yes.

8 Q. Which seems a reasonable enough request, doesn't it?

9 A. Yes.

10 Q. Yes. There is some flexibility here. This is Mr Pettet
11 from BPL. He is saying that he has put aside some 8Y
12 for immediate dispatch to PFC and he has done so because
13 there might be some patients who don't strictly meet the
14 criteria for trial.

15 Then [\[SNB0075982\]](#). Dr Perry reports back to
16 Dr Boulton, 24 July 1986. BPL are happy to supply 50
17 vials, and they ask in return only some information on
18 what happens when it's used.

19 Then [\[SNB0075984\]](#). Dr Perry back to Dr Smith at
20 PFL, accepting the offer.

21 [\[SNB0075986\]](#). Dr Perry to Mr Pettet, 28 July 1986,
22 firming up the arrangements and that the supply is
23 conditional on users participating in the clinical
24 trial. Although we have noted that Mr Pettet wasn't
25 insisting on that, he was saying you might need it for

1 patients who don't, strictly speaking, satisfy the trial
2 criteria.

3 So the 50 vials are coming as a contingency stock of
4 non-infective material in the unlikely event that
5 a virgin haemophiliac presents for treatment in the near
6 future.

7 [\[SNB0075990\]](#), please. 1 August. Dr Smith to
8 Dr Perry:

9 "I am sending attached 50 vials of 8Y, in case you
10 wish to protect category 1 patients before your Z8 is
11 ready."

12 Category 1 patients? Is that some sort of English
13 designation? You don't recognise the term?

14 A. I don't recognise the term but I would guess it's
15 patients who have never previously been transfused with
16 blood or blood products.

17 Q. Right. [\[SNB0076022\]](#).

18 THE CHAIRMAN: I was just looking at the last paragraph,
19 suggesting that the discussions had lit some very long
20 fuses. Were you expecting some sort of explosion in the
21 future? It's just a comment.

22 MS DUNLOP: Right. [\[SNB0076022\]](#) I think we were at. Yes,
23 thank you.

24 That's Dr Perry asking Dr Boulton to let him know
25 the batch of Factor VIII involved in the transmission of

1 NANB hepatitis to Dr Ludlam's virgin patient:

2 "While this outcome of treatment is not surprising,
3 we need to know the batch number and dose to keep our
4 surveillance cross-referencing records complete."

5 [\[SNB0076024\]](#). Dr Perry to Dr Boulton on
6 5 August 1986, saying that:

7 "The 8Y has now arrived from BPL and I have sent 20
8 vials to your centre. There is more here if you need
9 it. I enclose the BPL trial protocol and pro forma for
10 clinical data, since it has been supplied on the strict
11 understanding that data will be collected if the product
12 is used."

13 Just to finish this sequence, [\[SNB0076048\]](#). This is
14 Dr Perry bringing Dr Boulton up to date on 7 August 1986
15 to say that:

16 "PFC have now successfully manufactured two batches
17 of a heat-treated Factor VIII, treated at 80 degrees for
18 72 hours, and they are looking to make it available for
19 clinical trial at the end of August/beginning
20 of September."

21 So a new Scottish product more severely heated is
22 definitely on the way, and I don't want to go too far
23 into that because that's our next topic, but we have
24 looked at that little chain of correspondence from the
25 summer of 1986, which resulted in the obtaining of 50

1 vials of BPL 8Y. PFC obtained it and they sent you
2 20 -- well, not you but they sent to Dr Boulton, 20 for
3 storage in the Edinburgh transfusion centre.

4 Can we then please go back to the appendix document,
5 [\[PEN0171798\]](#). And at paragraph 10 there is your summary
6 of the request for the 8Y and the grant of that request.

7 Professor Ludlam, we have looked at a lot of
8 material and it certainly seems, particularly from the
9 early letter in that sequence, 27 June 1986, as though
10 you had first mooted the possibility of getting some 8Y
11 some weeks before the date of that letter, which is
12 27 June 1986. You said you thought that might have been
13 that you had heard something perhaps from Dr Perry's
14 report or one of your colleagues in Scotland about the
15 8Y product.

16 The circumstances in which a patient had been
17 treated with Scottish heated concentrate and appeared to
18 have developed symptoms of non-A non-B Hepatitis, did
19 that, as it were, resurrect that thought in your mind?
20 You might have had it a little before, that it would be
21 an idea to obtain some 8Y for patients who had not
22 previously been exposed and then that very thing
23 happened: someone was given treatment and developed
24 symptoms of non-A non-B Hepatitis. Did that sharpen
25 your focus on trying to obtain some 8Y?

1 A. To be honest, I'm not certain which way round it
2 occurred. I think it was in my discussions with the
3 blood transfusion colleagues after it had happened, that
4 the real potential, possible extra safety of 8Y was
5 being highlighted in my mind.

6 There was the view around that England was desperate
7 for every bottle of 8Y it could get. It had been very
8 deprived of heat-treated concentrates, NHS heat-treated
9 concentrates, for the first two thirds of 1985, when
10 there was all the anxiety about HIV transmission, and
11 there wasn't a BPL product that was heat-treated, unlike
12 we had in Scotland. They had unheat-treated commercial
13 concentrate and so there was a big -- I'm not sure it's
14 the right word -- yearning to have a heat-treated NHS
15 concentrate in England.

16 They were feeling this was really very important,
17 and I got the impression that every bottle of it was
18 being treasured and valued and I wasn't at all certain,
19 even if I had wanted some, I would have been able to get
20 some, and I think that's why we went through the
21 Bob Perry formal SNBTS channels, because that was likely
22 to carry greater leverage than if I had written as
23 a single clinician to BPL.

24 So I'm sorry, I can't remember exactly how the
25 sequence of thoughts went. But certainly this sad

1 episode of a patient susceptible to non-A non-B had
2 acquired non-A non-B who had highlighted the issue.

3 Q. If it had been you personally looking after the patient
4 concerned, and if you had had a stock of 8Y already
5 there, would you have used it?

6 A. In June 198 --

7 Q. I think we are actually talking about May 1986?

8 A. May 1986?

9 Q. Yes.

10 A. If I had had 8Y available in the fridge and I had
11 personally been assessing someone who I thought should
12 be treated with a clotting factor containing
13 Factor VIII, then I think I would have been very tempted
14 to use it.

15 Q. Yes. It sounds as though your purpose in the summer of
16 1986, in trying to get some 8Y, was for just such
17 a patient?

18 A. Yes.

19 Q. Can we then look at paragraphs 11 to 13, and I think we
20 can take this quite shortly.

21 You have mentioned the uncertainty which was present
22 in 1986 about the efficacy of dry heat treatment. You
23 have mentioned the FDA. Although they seem to have had
24 something of a change of heart.

25 A. Two years later.

1 Q. Yes. Then you have gone on to talk about Z8 and as
2 I have already said, we are not quite there yet, so I am
3 afraid that will have to wait for your next appearance.

4 Can we then go back, please, to the statement? That
5 document is [\[PEN0171790\]](#).

6 We were at the second page and in paragraph 5 you
7 are again talking about Z8 and in paragraph 6 you draw
8 a contrast with the position in England. I suppose, if
9 we are comparing Scotland and England at this time --
10 and that's an exercise in which we do fairly often
11 indulge -- we have one country with enough heat-treated
12 product but not quite severely heated enough, and the
13 other country with product which is severely heated
14 enough but not enough of it.

15 A. For some of the time.

16 Q. For some of the time.

17 Much of the next section of your statement has
18 already been covered. You talked here about the aim of
19 preventing HIV transmission, which we understand. You
20 mention the circular of 14 December 1984 by
21 Professor Bloom. Paragraph 8, I think we can move over.
22 Then on to 9, which is entitled "Risks/Benefits of
23 Cryoprecipitate".

24 You tell us, professor, that:

25 "Once the lifetime patient exposure to

1 cryoprecipitate reached approximately 100 donors, about
2 five infusions in an adult, the risk of non-A non-B
3 Hepatitis approached 100 per cent."

4 That is taking a 1 per cent incidence, is it?

5 A. It is, and perhaps I'm a little pessimistic. Perhaps we
6 could make it 200 donors, but whether it's 100 or 200,
7 you get there very quickly.

8 Q. Yes, I think we can perhaps cut matters short because
9 that was going to be the next bit.

10 We have looked, and we don't need to do so now, at
11 a paper by Minor and others, which gives an incidence of
12 0.4 per cent. We have also looked at Professor Thomas's
13 map of the world, where we can see a different incidence
14 as between North America and the United Kingdom.
15 North America is green and the United Kingdom is blue,
16 denoting that the incidence in North America is at least
17 double what it is in the United Kingdom, although that
18 map is 1999.

19 You go on, slightly lower down, to talk about the
20 relative risks that, certainly in the period
21 until October 1985, donors were not tested for HIV,
22 HTLV-III antibodies, as I suppose it would then have
23 been called. So there is that problem, and then we also
24 understood about the window period, which even the
25 introduction of screening in October 1985 did not meet.

1 You go on to say:

2 "During the period 1984 to 1987, if only a single or
3 very occasional treatment with a blood product was
4 required, it could be argued that cryoprecipitate was
5 safer with respect to non-A non-B Hepatitis, than
6 heat-treated NHS concentrate. The disadvantage of
7 cryoprecipitate, however, was that it was not
8 heat-treated and therefore could transmit HIV."

9 We have already looked at Professor Lowe's article
10 with Professor Lowe and I thought perhaps I would ask
11 you just to look at it too. It's [\[SNB0015523\]](#).

12 I expect you have seen this before too,

13 Professor Ludlam?

14 A. Yes.

15 Q. We know that Professor Lowe had been asked to submit an
16 article on AIDS and haemophilia for an edition of the
17 Scottish Medical Journal which was devoted to AIDS, and
18 this is his contribution.

19 The particular passage begins at the bottom of
20 page 2, if we could go to that, please. He is looking
21 at different therapeutic options. He lists various
22 precautions which can be taken to prevent further HIV
23 infection of patients with haemophilia. Firstly the
24 screening of donors. Well, donor selection, I should
25 call it. Then secondly, clotting factor concentrates

1 have been heat-treated since 1985.

2 Sorry, to be strictly accurate, the first option is
3 both selection of donors and screening of donations, the
4 second, heat treatment of clotting factors, and then can
5 we go on to the next page, please:

6 "A third means of reducing the risk of HIV infection
7 is to use lower risk treatments than clotting factor
8 concentrates where possible. This policy should also
9 reduce the risk of viral hepatitis, which is not
10 prevented by heat treatment of concentrates."

11 I suppose -- and I'm conscious that Professor Lowe
12 is still here -- one might, if one were being pedantic,
13 slightly challenge the wording of the first sentence
14 because, so far as HIV risk is concerned, the fact that
15 all NHS concentrates in Scotland were heat-treated might
16 mean that it wouldn't necessarily be a way of reducing
17 the risk of HIV infection to use other products.

18 So if one were thinking solely of HIV infection, the
19 use of something like cryoprecipitate, as against
20 a heat-treated clotting factor, might be debatable but
21 certainly, as far as hepatitis is concerned, he is
22 making the point that there are other treatment options,
23 including cryoprecipitate, fresh-frozen plasma,
24 desmopressin, and so on.

25 Would you agree with the views that he is

1 expressing?

2 A. I would just add that cryoprecipitate only reduces the
3 risk of viral hepatitis if you give treatment or
4 a therapeutic dose from a few donors.

5 Q. Yes.

6 A. If you give --

7 Q. If you are up at 200 donors?

8 A. An average adult dose is from 20 donors. If you give it
9 twice a day, that's 40 donors you have been exposed to
10 in a day. So if you give a course of treatment for five
11 days, you have almost certainly got non-A non-B
12 Hepatitis at the end of that. But if you need to give
13 just a single treatment on one occasion, then the risk
14 of hepatitis will be less.

15 Q. Yes.

16 A. But you might give single treatments on different
17 occasions, spread out over several years, and that is
18 still cumulative.

19 Q. Yes.

20 A. But for a single treatment occasion cryoprecipitate has
21 a lower risk of transmitting non-A non-B Hepatitis than
22 most of the heat-treated concentrates.

23 Q. Right.

24 I'm conscious, sir, that it's quarter past three.

25 I do have a few more questions for Professor Ludlam and

1 perhaps rather than rushing them, it might be an idea to
2 have a break now?

3 THE CHAIRMAN: I don't want to be rushed. I think it would
4 be better to have a break.

5 MS DUNLOP: Yes.

6 (3.15 pm)

7 (Short break)

8 (3.36 am)

9 MS DUNLOP: Professor Ludlam, just one or two more
10 questions. In your statement, [\[PEN0171790\]](#), at
11 paragraph 10, which is on 1793, you address the question
12 of numbers and there is a relevant passage in the
13 preliminary report. We have actually already looked at
14 this but just to have a quick look at it again. It's
15 pages 328 to 329 in the preliminary report, which is
16 [\[LIT0012543\]](#) at page 79.

17 It's this little section between 9.323 and 9.326.
18 We can see that in 2000 there was some exploration of
19 different statistics, the number of Hepatitis C positive
20 haemophilia patients for the different centres, and then
21 9.325, on to the next page, deaths since
22 1 September 1985.

23 Then 9.326, the number of people treated for the
24 first time in Scotland with a blood product, during the
25 period from 1 September 1985 to 30 June 1987. Some

1 figures are given: 18 for the East of Scotland and 13
2 for the West of Scotland. Do you happen to know,
3 Professor Ludlam, if the East of Scotland goes all the
4 way to the top, as my learned friend puts it. Does that
5 mean Edinburgh, Dundee, Aberdeen or does it mean just
6 your centre?

7 A. It means to Kirkwall and Shetland.

8 Q. Right, yes.

9 THE CHAIRMAN: I think that's certainly what it was intended
10 to mean because 9.324 in brackets does have a definition
11 of the east coast centres.

12 MS DUNLOP: East coast centres, yes, right.

13 THE CHAIRMAN: And that is the way it was looked on in fact,
14 is it, professor?

15 A. Yes.

16 MS DUNLOP: Right. Can we just go back then to the
17 statement, please, 11, therapeutic options you have set
18 out.

19 On to the next page, please. This is obviously
20 during this period, December 1984 to May 1987; children
21 with severe or moderate Haemophilia A were treated with
22 cryoprecipitate or heat-treated Factor VIII and we
23 understand the relative risks of the different products.

24 In making that choice between cryoprecipitate or
25 heat-treated Factor VIII, would that depend on factors

1 peculiar to the individual patient and the individual
2 situation?

3 A. It would depend upon the frequency of treatment. There
4 are some moderate haemophiliacs who bleed very
5 infrequently, usually come up to hospital for treatment
6 and one might give them cryoprecipitate. There are
7 other patients with moderate haemophilia who would bleed
8 really quite frequently and we put on to home treatment,
9 and that's often the trigger for putting them on to
10 concentrate.

11 Q. During this period, if you had been dealing with a small
12 child and the Factor VIII levels had been very low or
13 quite low, so I suppose severe or moderate, would you
14 have wanted to try cryoprecipitate first, because
15 I suppose you don't have an idea at all how frequently
16 this child is going to bleed?

17 A. You mean the first time they present with a bleed?

18 Q. Yes.

19 A. One would probably have treated them with
20 cryoprecipitate. Having said that, there would be some
21 haemophilia centres who would treat them straight away
22 with concentrate for reasons that have been thought
23 about here before, because they are going to get
24 concentrate after a very short while, in terms of years,
25 they are going to get Hepatitis C out of the

1 cryoprecipitate after they have received a few
2 infusions.

3 Q. I suppose, though, what might be in the mind of
4 a treating clinician would be that this is, one would
5 hope, a short period until a safer concentrate might
6 become available. So it might be a question really of
7 tiding them over until a better product arrived?

8 A. I'm sorry, thinking about this particular period, yes,
9 there is a slightly stronger argument for using
10 cryoprecipitate.

11 Q. Yes. And then when you talk about the risks that attend
12 cryoprecipitate, you mention the potential risk of HIV,
13 as it was an unheated product, but the magnitude of that
14 risk perhaps would be low because it would mean, if
15 cryoprecipitate transmitted HIV, after October 1985 at
16 any rate, when the donations were screened, it could
17 only be because an infected donation had somehow got
18 through, either because the screening test had failed or
19 because the donor had donated in a window period?

20 A. Yes.

21 Q. Yes. In this period, the end of 84 to 87, with
22 patients, would you have been taking the patient into
23 the discussions with you? So with children, would you
24 have been discussing it with the parents and with older
25 patients, discussing it with the patients themselves,

1 all these different possibilities?

2 A. Yes.

3 Q. Right. And trying to explain to them in a way that they
4 could follow what the relative risks were?

5 A. I hope so. That's what we intended to do. Over the
6 period 1984 to, say, 1988, a slightly longer period,
7 cryoprecipitate was used decreasingly often.

8 Q. Right.

9 A. Partly because we were able to offer, I think, better
10 home treatment service and get people out of hospital
11 and not having to come up to hospital.

12 Q. Right. Did you continue to stock it, though.

13 A. Oh, we stocked it, yes.

14 Q. Right. Then you set out under the heading at (b), the
15 options for those with mild haemophilia and
16 von Willebrand's disease, and I think we recognise
17 these: to manage without the use of a blood product, and
18 you remind us of the increased trouble that patients can
19 experience if a bleed is left for a while untreated.
20 DDAVP, I think we have talked about a lot already, and
21 we have had the views of Professor Lowe on this too.

22 Onto the next page: another option, cryoprecipitate
23 occasionally for treatment of Haemophilia A or
24 heat-treated Factor VIII, and then you are saying that
25 after August 1986, 8Y was available for virally naive

1 patients presenting with a major bleed. When the
2 initial stock was used up, a further supply was obtained
3 from Newcastle. So obviously you did use those 20
4 vials?

5 A. We used them, not in a previously untransfused patient
6 but I think in another patient who had allergic
7 reactions to the Scottish product.

8 Q. Right. What happened to the other 30, do you know? Did
9 you get them in due course?

10 A. I suspect we used those and when those were used up --
11 I'm sorry, I don't know, you would need to ask blood
12 transfusion issue departments.

13 Q. Don't worry.

14 You have talked also in paragraph 12 about the
15 therapeutic options for Haemophilia B, and we understand
16 that a slightly different picture obtained there. We
17 know that there was the gap between December 1984
18 and October 1985 for Factor IX?

19 A. Could I correct this? It is in fact August 1985 --

20 Q. Right.

21 A. -- that it became available.

22 Q. Yes.

23 A. The middle of August.

24 Q. Right. And we actually know that in Glasgow
25 in April 1985, they decided to buy heat-treated

1 commercial Factor IX. You didn't do that?

2 A. No.

3 Q. Just on this whole question of the different options for
4 treatment -- and this has obviously been a difficult and
5 anxious exercise, trying to define different therapeutic
6 options and point out the advantages and disadvantages
7 of each and in what patients one might be more suitable
8 and so on -- can I ask you to take a look at the
9 transcript, and I would like to go back to May, when you
10 came to give evidence, in block 2. Transcript
11 TRN0010018.

12 THE CHAIRMAN: Which day is it, please?

13 MS DUNLOP: This is 3 May.

14 THE CHAIRMAN: No, which day? It helps me to find the
15 material if I know the day. 18?

16 MS DUNLOP: Day 18? Right, thank you.

17 On Day 18, when you were, I think, giving a much
18 bigger contribution than you had on the previous visit,
19 when you had only talked about statistics. We took some
20 basic information from you. Can we go to the third
21 page, please? I think at this point I'm going through
22 your CV. Anyway, looking at about line 10, there is
23 a question:

24 "... referrals from other Scottish centres with
25 which you worked closely, and there is a, I think,

1 elsewhere, in relation to networking of systems, mention
2 of the East of Scotland. Are you in Edinburgh connected
3 to centres in Dundee and Aberdeen? Is that right?

4 "Answer: Yes, we are the comprehensive care centre
5 for the East of Scotland ... "

6 We are back to how far up does it go and you tell us
7 it goes to Dundee, Aberdeen and Inverness:

8 "So Glasgow doesn't have a tertiary function in
9 relation to any of the other centres in Scotland,
10 I suppose, apart from Yorkhill?"

11 You go on to say that the situation is a bit
12 flexible. Some patients come by plane and it depends
13 a bit where the plane lands, but you say:

14 " ... in general, for administrative reasons, I have
15 responsibility for trying to provide the service in the
16 East of Scotland ...

17 "Question: Is that a longstanding arrangement that
18 you have additional, as it were, tertiary
19 responsibilities for the centres further north?

20 "Answer: Yes, that's a longstanding arrangement."

21 Then if we look at 62, we can see another reference
22 to this status as reference centre, and I'm quoting from
23 some minutes where unofficially Glasgow and Edinburgh
24 acted as reference centres. This is 1980.

25 Let me just go a little bit further down. You said

1 you were keen that Edinburgh and Glasgow were seen as
2 reference centres, you were part of a UK arrangement for
3 overseeing haemophilia treatment. What steps did you
4 take during this period, end of 1984 to 1987, to give
5 guidance to people in Dundee, Aberdeen, Inverness and
6 points beyond?

7 A. The position of haemophilia centres in Scotland has been
8 a slightly unusual one, as I pointed out in these
9 quotations. Edinburgh and Glasgow were keen to be seen
10 as reference centres, along with similar services in
11 England and Wales, so that we could be a part of the
12 network and keep in touch with what was happening
13 elsewhere in the country.

14 There was quite a lot of discussion about --
15 particularly with the Scottish Office, you may recall,
16 about what our position was because in the original
17 health circular, all the haemophilia centres were seen
18 as equal centres, and so there was not quite -- in those
19 days -- and this was before we started having regular
20 meetings -- the centres in Scotland, I think, were seen
21 as part of a UK network.

22 Q. Yes.

23 A. More so, I think, than, if you like, a network of
24 centres in Scotland. And it was a way of addressing
25 this situation, amongst a number of other things we

1 wanted to progress, was setting up what started out as
2 the Factor VIII working party in 1988, and that
3 progressed into a more general working party for the
4 exchange of information and views about how haemophilia
5 services should be managed and what products were
6 available, and so on.

7 Before that, the centres were much more independent,
8 standalone centres and there was not a great deal of
9 interplay between them. Occasionally I would get
10 a phone call about a difficult patient or something that
11 was causing a difficulty or a problem, but there weren't
12 regular meetings like there are now, where we meet every
13 two or three months.

14 Q. Right. You did use the word "overseeing" but it seems,
15 from what you are now saying, as though, at least in the
16 mid 1980s, it was more of a reactive role. So if
17 somebody phoned you up for advice, you would be happy to
18 provide it?

19 A. Yes, I think it evolved from being very separate,
20 individual centres until the mid-1980s and, as a result
21 of the development of all these new products and the
22 need to test them, for one reason, brought us together
23 to collaborate more.

24 Q. Right. That document, the December 1984 document, which
25 you have told us was really written by Professor Bloom

1 but which was the product of discussions amongst the
2 reference centre directors, how would that get
3 to Dundee, Aberdeen and Inverness?

4 A. From Oxford.

5 Q. Right. So you didn't take any part in issuing guidance
6 or advice proactively to the other centres that, at
7 least nominally, were underneath you. You were
8 a tertiary centre and they are secondary. You didn't
9 take any part in distributing guidance or advice to
10 them?

11 A. No, the information was not cascaded down through us in
12 Edinburgh to other centres; it came directly from UKHCDO
13 secretariat in Oxford, who sent all these circulars that
14 had been discussed, even the ones that had been
15 addressed to me personally, in fact, had my name typed
16 in because they were carefully done, they all came to
17 each of 100 haemophilia centres in the UK individually.

18 Q. Okay. So, just to take it one stage further, how would
19 a doctor in a small hospital in, say, Stornoway, get
20 their guidance?

21 A. They would -- there isn't a haematologist in Stornoway,
22 as far as I know.

23 Q. No, but there will be people with haemophilia?

24 A. Yes, absolutely. They, as individuals, once diagnosed,
25 are, I think, usually looked after in Glasgow because

1 the flights go from Stornoway to Glasgow Airport,
2 although they may get -- may have had some link with
3 Inverness. They got their supplies of Factor VIII, when
4 it was supplied by the Blood Transfusion Service, from
5 Inverness on the bus and then the ferry.

6 Q. Right. Okay. But Oxford isn't going to send the
7 guidance advice to Stornoway, so how, physically, is the
8 hospital in Stornoway to receive advice on which it may
9 have to draw if it has to deal with a patient with
10 haemophilia?

11 A. If it has a patient with haemophilia, it would -- the
12 clinician in Stornoway would either use his best
13 judgment or he might get advice from -- by telephone
14 from Inverness or Glasgow.

15 Q. Right.

16 THE CHAIRMAN: Professor, did you have any authority over
17 any other haemophilia clinician in Scotland at this
18 time?

19 A. No.

20 THE CHAIRMAN: And no one would have been obliged to ask you
21 for instructions or for advice? Is that the position?

22 A. I think that's correct, yes. If they wished to, they
23 could but I certainly couldn't dictate what went on in
24 any of these other centres.

25 MS DUNLOP: Indeed. So what then is the point of Oxford

1 sending the guidance document to all the centres? If
2 everyone is autonomous, what's the point of sending the
3 guidance document around? It's to help, isn't it?

4 A. It is to help. It's for guidance.

5 Q. Yes, right.

6 THE CHAIRMAN: But of course, guidance only managed to break
7 out of the meeting of the haemophilia reference
8 directors if they all agreed, because otherwise they
9 didn't have any authority over each other, did they?

10 A. I think that's fair. We worked on consensus. There
11 were always people -- there was a range of therapeutic
12 practice and a range of views, and that was played out
13 in the country.

14 MS DUNLOP: Yes, but we have seen that from time to time --
15 and this is obviously a good example because it was
16 a very serious situation -- it was possible to publish
17 a consensus document, no doubt recording, as that one
18 does, that individual circumstances will have to be
19 assessed by individual directors, but sketching some
20 broad parameters and perhaps explaining different
21 options that might be available.

22 A. Yes.

23 Q. So really, for a centre in a remote part of Scotland, if
24 one can call it that, perhaps a less populous part of
25 Scotland, which is not a haemophilia centre but which is

1 suddenly confronted with a person with haemophilia who
2 needs treatment, there isn't necessarily any guidance on
3 which they can immediately draw because it's unlikely
4 that anyone has sent it to them, or if they have it will
5 be a sort of initiative of any particular individual,
6 and I think what you are telling us is that the person
7 in the less populous area, the clinician, is going to
8 have to ring someone to get advice. So it's really
9 dependent on their initiative in making contact with
10 somebody.

11 A. Well, it usually depends upon the clinical
12 circumstances. If a patient gets off the ferry in
13 Stornoway, a known haemophiliac, knows what his
14 treatment is and has an ankle bleed and goes to the
15 hospital and asks if they have got some of that
16 treatment they have in the fridge, then it's fairly
17 straightforward.

18 Q. Yes.

19 A. The physician may have experience of treating other
20 patients with haemophilia in Stornoway. I'm sorry,
21 I don't know.

22 Q. I think I'm just suggesting, professor, that it might
23 happen that a generalist, as all doctors in very remote
24 hospitals have to be, maybe in Stornoway or Kirkwall or
25 Lerwick, it might have been a while since they last saw

1 a virgin haemophiliac patient and they might need a bit
2 of help.

3 A. It is likely that they may never have seen a virgin,
4 non-transfused haemophilia patient because there are so
5 very few, as we have been discussing. We see about one
6 a year in --

7 Q. So it's not a common occurrence for you?

8 A. It's not a common occurrence for us and it would be
9 uncommon, as a new patient, in somewhere like Stornoway.

10 Q. So in that situation, although obviously we are purely
11 talking hypothetically, you would think it would be
12 quite likely that such a doctor would want to seek some
13 advice?

14 A. Probably.

15 Q. Yes.

16 THE CHAIRMAN: I'm quite worried. Professor James is
17 pointing out that to get effective advice, one has to
18 imagine, for example, taking a blood test, sending the
19 sample to the mainland to find out the Factor VIII level
20 before he could even begin to ask relevant questions, if
21 he understood what the relevant questions might be.

22 It is quite worrying, you see, I think that is what
23 is coming over from Ms Dunlop, not just in Scotland but
24 in the west, remember the last time we raised this --

25 MS DUNLOP: Yes, Devon and Cornwall.

1 THE CHAIRMAN: Yes, where one has remote communities, quite
2 capable of having haemophilia patients within them, they
3 may not have available locally the resources necessary
4 to ensure effective and prompt care of their patients.

5 Was there a mechanism? The answer appears so far to
6 be not much, if any, Professor Ludlam.

7 A. Yes, I'm sorry, I don't know enough about the laboratory
8 expertise in Stornoway, as to whether they can measure
9 Factor VIII levels, for example. But if there was
10 a small child presenting with a bleed that was thought
11 to be haemophilia, well, maybe they would be transferred
12 to Inverness, would be the sort of usual -- or flown to
13 Glasgow.

14 Q. Right.

15 THE CHAIRMAN: Nowadays we would expect them, I think, to go
16 in the helicopter just because the risks would be there
17 and one would wish to counter them, but perhaps in the
18 period we are thinking about, it might have been
19 Caledonian MacBrayne, and that would only be if it was
20 running given the weather. Not a happy situation.

21 A. I think it would have been possible to get a child out
22 of Stornoway, to either Inverness or Glasgow, within
23 12 hours.

24 THE CHAIRMAN: Right, and would that be, in your view,
25 a sort of sufficient period in most cases or all cases?

1 A. I think so. The child would be jolly uncomfortable and
2 distraught with a swollen knee joint probably, but if
3 you haven't got a Factor VIII or Factor IX measuring
4 facility in your laboratory, and they may or may not
5 have, then you can't make the diagnosis.

6 MS DUNLOP: Yes.

7 A. Maybe they can measure clotting factors in Stornoway,
8 but even then they may not do them very often, and
9 therefore the reliability of the result might be not as
10 good as it would be in a laboratory that's doing a lot
11 of them.

12 Q. Yes. I mean, these centres of population, Stornoway,
13 Kirkwall, Lerwick and so on, they do have hospitals, of
14 course they have hospitals but necessarily, the
15 clinicians who staff them have to know about a very
16 broad range of different medical conditions because
17 I suppose they never know what tomorrow might bring. So
18 the chances of them being very up to speed on
19 haemophilia care might be slightly less.

20 A. All the more so because it is increasingly being
21 centralised into haemophilia centres.

22 Q. Even in the mid 1980s?

23 A. Even in the -- well, we heard several months ago, in
24 this forum, about patients coming from outlying
25 hospitals into -- particularly Glasgow, and the same

1 thing happened in the East of Scotland, into centres
2 that were more used to dealing with the patients and
3 therefore hopefully could offer a better service.

4 Q. Yes. Professor Ludlam, it's five past four, so I'm only
5 going to ask you about one more thing.

6 I said we would be coming back to this and it's the
7 whole notion of recall. Dr Perry has drawn to our
8 attention a terminological problem, in that I think he
9 would prefer if we used the term "exchange", and we do
10 know that the first such exchange occurred
11 in December 1984, when unheated product was recalled and
12 replaced with heated product. He has provided
13 information on this topic.

14 Can we just have [\[PEN0120866\]](#), please?

15 THE CHAIRMAN: While that's being obtained, your question
16 actually put together the two elements of an exchange
17 that I would have thought were proper, and the first was
18 recall. Is there some significance in the substitution?

19 MS DUNLOP: To be fair to Dr Perry, who isn't here, he says:

20 "The term 'product recall', when applied to
21 pharmaceutical and other products, normally describes
22 actions taken in response to the discovery of a known or
23 suspected defective product. In this respect, the
24 actions taken by SNBTS are better described as 'product
25 exchanges'."

1 THE CHAIRMAN: All right, if it's that sort of worry he has,
2 we might well just accommodate him, but I have to say,
3 it doesn't seem to be the most important thing that I'm
4 going to have to think about. Yes, "product recall",
5 one knows, is used in a particular context.

6 MS DUNLOP: This document deals with more than recall of
7 stocks but just to look at the third page from here,
8 there is a table, which is quite a useful summary of
9 what happened. We see "superseded products" shown and
10 then "New product", "Product exchange/recall",
11 "Rationale" and "Comments".

12 Because it's late, just to summarise what seems to
13 have happened, that in December 1984 there was a like
14 for like exchange, or a like for unlike exchange. There
15 was a return of unheated product and a replacement with
16 heated product. When the change was made to product
17 heated for 24 hours, rather than product heated for two
18 hours, there wasn't initially an exchange but there was,
19 in the autumn of 1985, a recall, an exchange, and
20 I think, rather than asking you about the details of
21 this, which are all set out for us, I just wanted to
22 find out from you, as a haemophilia director, how
23 physically you got the product back.

24 A. In December 1984 I contacted people and asked them to
25 bring back their unused, unheated product.

1 Q. So someone telephones patients?

2 A. Yes.

3 Q. Not you?

4 A. Not me fortunately --

5 Q. Someone in your department?

6 A. Yes, probably our haemophilia sister. And I have

7 actually looked at the records for this month recently.

8 The new product was first issued on 14 December, so

9 all product issued after 14 December was heat-treated.

10 The two hours, 68 degrees.

11 There was actually very little product brought back

12 because Factor VIII was so scarce that we only issued

13 home treatment batches of ten bottles at a time, which

14 was about enough for three treatments, and so a patient

15 might use that up in a fortnight.

16 Q. Right.

17 A. So by the time we phoned them, they said, "I have only

18 got one injection left and I need that now because I'm

19 bleeding," or, "I might need it before I can come up

20 next week, or whenever, to get the new product," but

21 everyone had new product with them by 28 December. So

22 for a two-week period everyone had been issued with new

23 product.

24 Q. Right. And was that same sort of approach followed on

25 subsequent occasions, when an exchange was being

1 arranged, that contact would be made with the patient by
2 somebody in your department and they would be told,
3 asked, to bring their product in and exchange it for the
4 new and better product?

5 A. Yes.

6 Q. Is that right?

7 A. Yes. The line at the bottom about DEFIX,
8 I appreciate -- and I'm slightly hesitant to suggest
9 that Dr Perry's dates are not correct because blood
10 transfusion has got exceedingly good records, but we
11 actually did start to receive heat-treated DEFIX on
12 9 August.

13 Q. 9 August. I'm obliged.

14 A. And that was issued to everybody thereafter.

15 Q. Right. I should say, sir, that I do intend to go
16 through Dr Perry's statement on this. Dr Perry isn't
17 coming. We have given him a rest for the moment, but he
18 has supplied written information which I will be drawing
19 to your attention on this topic.

20 It was really only, Professor Ludlam, that since you
21 were more at the sharp end of the recovery of stocks
22 from patients, I wanted to establish from you how that
23 was actually effected.

24 THE CHAIRMAN: Could I ask you one supplementary question:
25 what about Aberdeen and Inverness? At the stage of

1 recall, did you have any part to play in recalling
2 products from other centres?

3 A. Oh, it was an agreed national arrangement.

4 THE CHAIRMAN: Yes. So far as you were concerned, your
5 department made arrangements to recall the material from
6 the Southeast of Scotland?

7 A. Yes.

8 THE CHAIRMAN: Did your department make arrangements to
9 recall material elsewhere?

10 A. No, but the other haemophilia centres, I'm sure, phoned
11 up their own patients and got the recall or --

12 THE CHAIRMAN: So it is back again to the question of the
13 administrative oversight and so on. So really you dealt
14 with your own area in this respect?

15 A. Yes, I think it was driven also by the blood transfusion
16 saying, "Please, we want the product back and here is
17 some of the heat-treated."

18 MS DUNLOP: I'm obliged, thank you very much,
19 Professor Ludlam.

20 THE CHAIRMAN: Right.

21 Professor Ludlam, there are two outstanding matters
22 as far as I'm concerned: one, the issue that I raised
23 before lunch, and I don't want you to provide an answer
24 to that now. You may want to look at it. But just to
25 remind you that the information I have so far is that

1 the blood product unit at the Royal Infirmary began
2 producing Cohn Fraction I material in 1951, and Dr Cash
3 and Dr Spencely produced data in an article that showed
4 the actual use of product from 1961 onwards, so that one
5 can see the pattern that first of all it was
6 fresh-frozen plasma and antihaemophilic globulin, or
7 antihaemophilic factor, with cryoprecipitate coming in
8 quite a bit later.

9 So the picture one has, looking at that, is that
10 there was a significant supply of concentrate of that
11 sort of primitive variety over 15 years or so before the
12 mid-1970s, when PFC Factor VIII came in. I have at
13 least one death, where this is a practical issue because
14 of the onset of cirrhosis relative to possible dates of
15 infection, and so I would be very pleased if you could
16 find anything that would bear on the issue of whether
17 there were indications of Hepatitis C, as it came to be,
18 before, bearing in mind that we know that all the
19 records of the time essentially related to Hepatitis B
20 and the prevalence of NANB hepatitis was only discovered
21 later.

22 So it's not a clean and easy topic but it did seem
23 to me that it was material to try to find out whether,
24 in fact, by the time one came to look at PFC
25 Factor VIII, there is a history that one cannot ignore,

1 that may have been generating Hepatitis C over some
2 considerable period of time.

3 Does that make the issue clear enough for you to
4 look at?

5 A. Yes, I think the original observations about hepatitis
6 go back to Rosemary Biggs in the 1960s.

7 THE CHAIRMAN: I don't want you to speculate or whatever.
8 I know you are coming back again. If you come back some
9 time and can help me on that, or even give me a note
10 about it, I would be pleased.

11 The other thing I wanted to ask about, and it is
12 something I have asked other haemophilia clinicians, is
13 this: and it's whether there is some sort of dislocation
14 between the theoretical position of giving lots of
15 advice to people and giving them choices, and the
16 reality that one might think had to happen from time to
17 time, that we take the child in Stornoway for example,
18 waiting 12 hours to get to a competent haemophilia
19 clinician. The child has the knee swelling, as you have
20 described, is distraught, as you described. The parent,
21 one would expect, would be responding similarly.

22 In reality, what happened when one confronted that
23 situation? Was there a great long explanation or was
24 the reality something different?

25 A. It is very difficult because all these situations are

1 very different and people's memory of what happened in
2 the distress -- both the distress in the patient, the
3 parent -- the physician trying to deal with a difficult
4 situation may have said all sorts of things that
5 obviously the parents are in no state to hear, and yet
6 maybe they have to be said. And there comes a time
7 when, in a sense, one has to use one's best medical
8 judgment.

9 THE CHAIRMAN: You see --

10 A. That's what I'm employed to do.

11 THE CHAIRMAN: My natural sort of suspicion, as
12 a prospective patient, I suppose, and certainly as
13 a parent and grandparent, would be to think that the
14 response of the parent of a young child, especially,
15 confronted with this condition, would be to say,
16 "Doctor, do what you think is right and get on with it,"
17 and that might be the end of it. Is that not so?

18 A. I think it's awfully difficult for these parents. You
19 know, they had a perfectly well child until 12 hours ago
20 and their world has turned upside down, and they are
21 just as you describe, "Please do what you consider
22 best". So one does, but along the way I try and explain
23 the difficulty the child is in and what the problem is,
24 what the consequences are of not doing anything, what's
25 available, what are the side effects of it, and then you

1 get on with the treatment of the patients. The parents
2 think that that's what should happen. But it's in
3 a very distraught environment for everybody.

4 THE CHAIRMAN: Including the clinician.

5 A. That's what I mean, yes, everybody.

6 THE CHAIRMAN: And so really, if one thinks about the risks
7 of error in recollecting observed events anyway, whether
8 it's what's heard or what's seen, and the problems of
9 the memory working on what has happened and
10 confabulation, as one of your colleagues put it, the
11 creation of a situation out of a mixture of memory and
12 an impression of what should have happened, it must be
13 extremely difficult to be confident as to what was
14 actually said to any individual patient or any
15 individual set of parents.

16 A. Well, I think -- I can only talk about my practice and
17 perhaps other people that I see working with me.
18 Confronted with a particular situation, like a new
19 patient, well, it's my responsibility to point out the
20 benefits and the drawbacks of the treatment. So that's
21 sort of part of my automatic -- one of the automatic,
22 things, if you like, I do. So it doesn't have to be
23 thought out carefully each time.

24 THE CHAIRMAN: So if one has a child with a complex compound
25 fracture of the thigh having fallen on a hill in Skye,

1 I can't imagine people spending very long talking about
2 theory. The child would be in theatre, anaesthetised,
3 and there would be attempts being made to reduce the
4 fracture very, very quickly. Is that not so?

5 A. Absolutely, but if that child is being given a medicine
6 that has potentially serious side effects, let's think
7 about -- well, there used to be an anaesthetic agent
8 that gave rise to hepatitis. I'm sorry, I forget how
9 serious the hepatitis was but it was certainly sort of
10 around. You might expect possibly, if it was a bad form
11 of hepatitis, if it gave permanent hepatitis, you might
12 expect the anaesthetist to mention it before the
13 anaesthetic.

14 THE CHAIRMAN: If the anaesthetist did, I'm not sure I would
15 expect the parent of that child to remember anything
16 about it.

17 A. I agree, that is -- you have put your finger on the
18 difficulty.

19 THE CHAIRMAN: Anyway, those are the two things I wanted to
20 ask you at this stage. It's 20 past four.

21 A. I'm sorry, we do give patients leaflets, you know. It's
22 a bit post hoc but there are things that people can take
23 away, maybe after they have had their first infusion,
24 but, you know, the Haemophilia Society is very active in
25 producing a lot of very good leaflets, for example,

1 because there is much more to haemophilia than the first
2 injection of Factor VIII.

3 THE CHAIRMAN: Yes. I won't make any comment on my cynical
4 response to leaflets as a way of helping people
5 understand. It might not be appropriate, but anyway,
6 I think we should stop and allow you to go for the
7 moment, Professor Ludlam.

8 Is it tomorrow Professor Ludlam is coming back?

9 MS DUNLOP: Just to explain, sir, what the story is about
10 tomorrow. We have Dr Colvin coming, he might not be
11 here sharp for half past nine but actually I think that,
12 I hope, will work quite well because obviously others
13 have to have the opportunity ask some questions of
14 Professor Ludlam. Professor Ludlam has very kindly made
15 himself available tomorrow anyway. So that, I think,
16 takes care of that.

17 The only other point to make is that there is
18 a procedural matter which I think counsel need to
19 discuss in front of you, sir, first thing in the
20 morning. So perhaps we can do that before
21 Professor Ludlam again takes the stand.

22 THE CHAIRMAN: Do you want to start early?

23 MS DUNLOP: No, I think there will be plenty of time. 9.30
24 will be perfectly adequate.

25 THE CHAIRMAN: Mr Anderson is showing obvious distress at

1 the thought of being here at 9 o'clock.

2 Very well, tomorrow morning then.

3 (4.24 pm)

4 (The Inquiry adjourned until 9.30 am the following day)

5

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