Tuesday, 26 April 2011

(9.30 am)

(Proceedings delayed)

(10.00 am)

THE CHAIRMAN: Good morning.

MS DUNLOP: Good morning, sir.

Introduction

Plainly, we have billed this morning as an opportunity for us to screen two episodes of World in Action and I imagine everyone is interested to see that.

I'm afraid I have some remarks. In this block for the next four weeks, we are only addressing topic B2, subject to a couple of qualifications which I will explain in a moment. Topic B2 is expressed as:

"The use of blood product concentrates in Scotland including any perceived disadvantages of such products from their introduction in or around 1974; the continuation of the use of commercial concentrates in particular, after international realisation that these carried a risk of AIDS; the proposal by Dr Galbraith of the Public Health Laboratory Service in May 1983 that use in the United Kingdom should be stopped and significant progress towards self-sufficiency in the manufacture of blood products by the NHS in Scotland had been made."

I plan to adopt a generally chronological approach to telling the story from the early 1970s to around the end of 1984. There are some exceptions to that: where a particular point needs to reach a conclusion then I will follow that piece of evidence to that conclusion.

I intend to lead 11 witnesses, five who are or were haemophilia clinicians, two who are or were transfusionists, the former national medical director of SNBTS, covering transfusion and fractionation, two scientists from the world of fractionation and an infectious diseases specialist.

Of course, so to describe them is to pigeonhole people and in fact there are considerable overlaps in the expertise of individuals, as will be seen. There are also individuals whose statements we will refer to but who are not giving evidence, mostly because the statements are of less importance or cover material covered by someone else who is giving evidence. In one or two cases people are not fit enough to come.

There will also be reference to some correspondence and it is my intention to use gaps, which will inevitably occur, to narrate some of these items. The scheduling has not been entirely easy to organise but I'm content that we have a reasonably logical order beginning with the haemophilia clinicians and moving to

those who represent the SNBTS, finishing with Professor Lever on infectious diseases. We may have some early finishes.

Mr Mackenzie will return on 12 May to lead the rest of the evidence from Dr Dow on topic C1, and that is my first qualification to the statement that we are only tackling B2.

The other qualification involves topic B5. As everyone knows, we have attempted to divide up the subject matter of the Inquiry into topics to make it manageable. Topic B5 is concerned more with the doctor/patient relationship and we intend to deal with that mostly in block 3 in June. But there are three witnesses whose evidence on topic B5 we propose to take in this block to save the time of the witnesses and the Inquiry. They are Dr Winter, Professor Hann and Dr Pettigrew.

Mr Gardiner will be leading evidence in relation to topic B5.

Turning more specifically to topic B2, there are certain themes I want to cover. Firstly, the arrival of commercial concentrates, although there were some earlier efforts to produce concentrates by the NHS in the 1960s, we understand that the commercial products, the first commercial products weren't available in this

country until the early 1970s. I want to look at attitudes within the government and of patients and haemophilia clinicians to concentrates around that time. I want to look at usage, the advantages and disadvantages of the products from time to time, risk/benefit assessments. I want to look at the provision of concentrates by the National Health Service in the 1970s and the 1980s, including the question of self-sufficiency for Scotland and whether it was or wasn't achieved. Did NHS products have similar drawbacks to commercial products? We will be looking too at the emerging realisation of the problem of AIDS in haemophilia. We will examine what was said by haemophilia clinicians mainly through UKHCDO, what was said by government and by the Haemophilia Society, as well as other actions of these bodies. We will look at the United States of America and at some other countries too.

We will also investigate the response to heat treated concentrates when those began to appear from 1983 and we will be trying to get an idea of government policy in Scotland in these areas.

With that brief outline, I would now begin to look at the evidence.

THE CHAIRMAN: Before you do that, can I make a comment?

I think, gentlemen, that it is very important that we should stick to the topics and not take the opportunity, as it might be seen, of having a particular witness here simply to ask questions more or less casually. If any party wishes to ask any of the witnesses who are to come a question that lies outside of the scope of the topics Ms Dunlop has mentioned, I will require that notice of that be given in writing in advance on this occasion. The informality that I allowed last term didn't work particularly successfully, on at least one occasion, and I'm not prepared to allow it to continue. So I'm going to stick to the rule so far as material outwith the scope of these topics is concerned. I hope that's understood.

MS DUNLOP: Before I begin to try to sketch some of the background from the early 1970s, I should record, sir, that there is, as you are well aware, a vast amount of documentation. A lot of the key documents are referred to in the preliminary report but there are some that have come to the attention of the Inquiry team since the preliminary report was published. So there are some extra documents, both for the 1970s and the 1980s.

This means that some of what we will be looking at in evidence is not in the preliminary report but I do want to put it before the Inquiry. In some cases that's

best done by putting a particular document to a witness who perhaps was around at the time or was at a particular meeting, but that's not always possible. Where it is not possible, I would propose simply to narrate a document or a meeting to draw it to everyone's attention, perhaps to put up the minutes or whatever. It's my hope and my belief that using that and the evidence of Dr Winter, Professor Ludlam and Professor Forbes in particular, we should be able to assemble a reasonably complete account of events, particularly between 1974 and 1984 in this area.

Sir, I suggest that the story, the story of the use of blood product concentrates, begins with the early realisation of the transmission of hepatitis by blood and blood products, firstly in blood, and if we could look at the preliminary report, this is real page, page 138, and [LIT0012431]. If we look in paragraph 6.2, this is the second sentence:

"The first association of blood transfusion with the development of hepatitis was recorded in 1943."

The article referred to there is in the Journal of the American Medical Association, 1943, by PB Beeson. There is also another reference which I would like to look at, [LIT0010246]. This is from the BMJ. It's dated December 1, 1945, and it is a letter which can be

seen on the left-hand side. It is headed up "Transmission of hepatitis during blood transfusion":

"It is an established fact that hepatitis, homologous serum jaundice, can occur 2 to 6 months after transfusion of human serum or plasma. In some episodes it has been possible to incriminate certain batches. In some batches the incidence of affected persons has been as high as 60 per cent."

The letter in fact goes on to discuss the possibility that in some instances it may be that icterogenic material was administered accidentally through syringes contaminated with icterogenic material, inadequately sterilised between injections, suggesting that one possibility could be that material is passed on through reuse of syringes or contaminated syringes. We are discussing something called a Higginson syringe.

Next I would like to look at the Maycock report, which is also referred to on page 138 of the preliminary report. This is [LIT0010063]. This describes the administration of human antihaemophilic globulin concentrate and three cases of homologous serum jaundice afterwards, all in 1958 and 1959, and we can see that if we look in particular at page 0081. There is a subheading "Homologous serum jaundice":

"Particular attention has been paid to the

occurrence of this complication in recipients of AHG concentrate. Among the patients reported here, three possible cases have been observed."

There is then discussion of those cases. Then under the heading "General":

"The use of human AHG concentrate has certain advantages. Compared with fresh blood or plasma, smaller volumes are needed to control haemorrhage and haemostasis is therefore achieved more rapidly, a fact of importance when haemorrhage is rapid and is causing extended tissue damage ... The clinical effect of AHG concentrate, since it has a known AHF content, is usually more accurately predictable than that of fresh frozen plasma ..."

Go on to the next page. We see that some of the potential difficulties in preparing concentrate on a large scale are anticipated.

Then the next reference is on page 138 of the preliminary report. If you go back to that. Footnote 2, reference to a letter by Whittaker and Brown "Serum hepatitis in a haemophiliac." BMJ1969 volume 3, page 597, which is [LIT0010248]. Perhaps if we don't go to that for a moment and look first actually at 0249, [LIT0010249], we can see that these are two publications in the BMJ quite close together. We see again this is

a letter headed, "Serum hepatitis in a haemophiliac", and this tells us that the Whittaker and Brown letter, was 6 September, page 597:

"Serum hepatitis is a rare but important hazard following the use of cryoprecipitated antihaemophilic globulin. We would like to report another non-fatal case."

We will see in a moment that Whittaker and Brown were reporting a fatal case. If we could now go to [LIT0010248], to Whittaker and Brown, we can see from the first paragraph of their letter -- well, firstly, a reference to an earlier report which is an American report, the New English Journal of Medicine in 1966 by Del Duca and Eppes. Which described:

"A 39-year old haemophiliac who developed transient jaundice 60 days after receiving 28 units of cryo ... we report a second case with a fatal outcome."

Then if we look at the last paragraph of what Whittaker and Brown said:

"Cryo represents a considerable advance in the management of the severe haemophiliac. This and other centres have used many thousands of units without mishap, and we do not know of a similar case in Britain. It is important to re-emphasise the potential danger of cryo, to ensure its use only when strictly needed.

A check should be kept of the source of cryo to trace any serum hepatitis which may occur in the future."

Then finally on this particular point -- that is on recognition of the transmission of hepatitis by blood and blood products -- I would like to look at a circular, which is [SNB0057275]. This is something called "Scottish hospital memorandum, number 89 of 1964":

"The Scottish National Blood Transfusion Association hospital blood transfusion arrangements and the supply of blood products in clinical use".

There is quite a lot of general introductory material about the organisation of the service. Then if we look to page 76, 7276, we can see that there is a subheading above paragraph 8:

"Hazards of blood transfusion":

"The hazards of transfusion therapy have become more widely recognised in recent years but avoidable transfusion accidents still occur in hospitals in Scotland."

Paragraph 9:

"The main dangers of transfusion therapy are (1) haemolytic reactions, (ii) bacterial infection, (iii) transmission of disease, (iv) iso-immunisation and (v) mechanical reactions ..."

Then on to the next page, SNB0057277, an important paragraph, sir, paragraph 11:

"All blood for transfusion must be regarded as potentially contaminated and care must be exercised to ensure correct conditions of storage. The supply is not only during storage in the blood bank but also during transportation. Bottles of blood must never be left unrefrigerated. The most important transmissible disease in this country is homologous serum jaundice or serum hepatitis, the incidence of which is five per 1,000 recipients of blood or small pool plasma. No transfusion should be undertaken unless the benefits outweigh the risk of hepatitis."

Then the subheading "Blood products in clinical use". Reading the second paragraph:

"As with whole blood, these products should be used only when there is a clear clinical necessity for the following reasons: (a), with the exception of gamma globulin and albumin, they may carry the risk of transmitting serum hepatitis. (b), large quantities of blood are required for their preparation and, (c) they are expensive to prepare."

In 1973 it was known that commercial concentrates were coming. I would like to look firstly at [DHF0012122]. This is obviously an English circular to

senior administrative medical officers headed up "Trends in the treatment of haemophilia":

"Antihaemophilic globulin concentrate is, in many instances, the therapeutic agent of choice in the treatment of haemophilic patients. The production of the human concentrate in the UK is at present insufficient to meet the stated needs of clinicians who care for patients requiring surgical, including dental, treatment, or who have episodes of severe bleeding. Considerably more of this preparation would be used if it were available. Product licences have very recently been granted to two firms ..."

I don't think it would be controversial if I were to say that those appear to be Immuno of Austria and Travenol, Hyland Travenol, of the United States:

"... which enable them to market foreign human AHG concentrate to hospitals and haemophilia centres in the UK. It has come to the notice of the department that one of the firms has already engaged in active promotion of this expensive product. The firm has indicated that they can supply large quantities of human AHG concentrate, and this could result in very significant expenditure if amounts were bought in excess of immediate needs.

In view of the several developments in the

management of patients with haemophilia, the department has decided to assemble a group of experts who will advise on likely trends in methods of treatment, possible future requirements for the treatment of the condition and the consequences for the supply of therapeutic agents, including human AHG concentrate."

So this is the expert group on the treatment of haemophilia. If we look at [DHF0012124] we see that someone -- and as usual we are not sure who, but someone in the Department of Health and Social Security is passing on a copy of this letter to senior administrative medical officers on the subject of trends in the treatment of haemophilia:

"The availability in this country of an American and an Austrian antihaemophilic globulin concentrate has made an urgent review necessary since, if a large proportion of eligible patients are to be treated with foreign commercially produced concentrate of this nature, the costs will probably amount to several million pounds a year. An expert group is being convened by medical division and will meet on 20 March. This group is to advise the department on trends in the treatment of haemophilia and it is anticipated that the conclusions reached will form the basis for future planning. Such planning could include consideration of

early arrangements for central purchase and controlled distribution of commercially produced concentrate, primarily to haemophilia centres, and the possibility in the slightly longer term of producing sufficient material in the UK to meet the need."

That's 13 March 1973. At this point, sir, I thought it might be useful to have a little bit of a look at who these companies are or were, and that is usefully explained by Douglas Starr. If we look in his book on blood at page 258, which is [LIT0012920] at 2928. This is a chapter entitled "The blood services complex", and we can see in the first full paragraph on page 258:

"Four major companies have controlled most of the world's plasma. Based in the United States, they included Cutter Laboratories of Berkeley, California, Alpha Therapeutic Corporation of Los Angeles, Armour Laboratories of Chicago and Hyland in a suburb of Los Angeles. These firms represented a pharmaceutical tradition. Armour, as we have seen, have been around since the previous century. Cutter, an old family business in northern California, boasted a colourful history of public involvement."

If we look down, actually, we can see a little bit of later development in the world of plasma, that in 1978 the Green Cross company of Japan bought

Alpha Therapeutic, and Green Cross also went on to buy part of a Spanish fractionator. Then in 1977, Bayer, a German pharmaceutical giant, took over Cutter; Armour passed from one owner to another until the French multinational, Rhone Poulenc, held on to it. Of the major producers, only one remained in the hands of Americans, Hyland, which itself had been purchased by Baxter Travenol Laboratories, a multinational healthcare conglomerate based in Chicago.

I'm referring to this, sir, because from time to time one sees all three of these names, Baxter, Hyland and Travenol, and it's useful to know that they are essentially all the same.

How was the news received in Scotland? Well, we need to look at [SNB0102011]. We can see that this document is the minutes of a meeting of the central consultative committee on blood transfusion at St Andrew's House on 15 March 1973. We can see that there were present some names we already recognise, Professor Douglas, I think Professor Forbes is going to come on to talk about, but a haemophilia clinician, both Professor Douglas and Professor Girdwood are indeed very well-known names. Also Dr George McDonald from Glasgow Royal Infirmary, Dr Iain Macdonald from SHHD; Dr Wallace, West of Scotland Blood Transfusion, and

Mr Watt of Protein Fractionation Centre all attending the meeting.

We can see that in fact there seems to have been a bit of difficulty about the content of the minutes of a previous meeting, if we look at the next page, SNB0102012, in paragraph 11 we can see that the central consultative committee had established its own working party to consider production, laboratory and clinical evaluation of the various Factor VIII and IX products in relation to the overall production capacity of the Blood Transfusion Service -- so NHS products -- and to report. There had been a working party meeting in September, a minute of the meeting had been circulated. There was some difficulty about the accuracy of the minutes. Then there is a bit of debate about that. Which I don't think it is really necessary to go into.

If we go to the next page, to paragraph 14 -- this is SNB0102013 -- we can see the situation was further compounded now because a commercial superconcentrate had been licensed for sale in this country at a high price. There was to be a meeting at DHSS on 20 March to discuss the matter.

Then back to the brouhaha. Dr Wallace said he had found the meeting helpful, regretted the subsequent history. He emphasised that time and effort were

required, not only for the design of effective trials but for the conduct of the trials. It was up to the BTS to produce a better concentrate than the commercial product.

Then paragraph 18:

"The department said that for the meeting with DHSS it was necessary to know the Scottish objective. It was hoped that there would be a step-up of production of Factor VIII, and in the meantime, although the commercial material might require to be used, it would only be in very small quantities. The situation was an evolving one."

19:

"PFC had, until recently, made Cohn Fraction I, which was not a good product but for a long time had been the only product. The facilities at Liberton would be more than adequate to provide all the Factor VIII products required."

One might think a slightly more ambitious steer on what was hoped for than we have seen in the DHSS document.

"It was possible that the meeting at DHSS ..."

This is reading from paragraph 20:

"... on 20 March would recommend the central purchase of the commercial concentrate for health

service use and that distribution should be through BTS centres. This would keep the situation under control and not allow a widespread market to be established through hospital pharmacies, it would also allow the BTS to step up its own production. The meeting agreed that if commercial concentrates had to be provided it should be by central purchase but that distribution should be made by the haemophilia centres, not through BTS centres."

Then we have the minutes of the meeting of the expert group on the treatment of haemophilia on 20 March 1973. This is [SNB0067631]. Again interesting to look at the dramatis personae. We can see Dr Rosemary Biggs who is obviously a very well-known name in the history of haemophilia treatment. Professor Douglas again, Dr Rizza, Dr Iain Macdonald from SHHD. Looking at the first paragraph:

"Several significant advances in the treatment of haemophilia have taken place in recent years. Various therapeutic materials are now available and most recently developed is human freeze-dried antihaemophilic globulin concentrate, which is expensive and may be in limited supply. Nevertheless, it appears to be the therapeutic agent of choice in the majority of cases and would be used widely if available in larger quantities."

It is narrated that the department -- this is DHSS:

"... have decided to assemble a group of experts to advise generally on what was happening in haemophilia treatment and to make proposals on which planning for the future could be based."

Terms of reference are noted. Then the size of the problem is discussed. Then on to the next page, 7632:

"Present treatment."

Dr Biggs had clearly produced a paper:

"It is agreed by clinicians that the preferred treatment of episodes of bleeding before and during surgical procedures is with the more purified products, namely cryoprecipitate and AHG concentrate."

Then a discussion of the various materials, cryoprecipitate, then the most commonly used therapeutic agent. Then freeze-dried concentrate. At the bottom of the page:

"It is presented in bottles, each containing about 400 units of Factor VIII activity."

At the of that paragraph:

"Adverse reactions following infusions of freeze-dried AHG concentrate are rare. A possible disadvantage arises from the fact that AHG concentrate is prepared from a larger pool of donations and in

theory, therefore, the risk of hepatitis is greater. About 1 in 800 of the donors who present to the transfusion service is a carrier of Hepatitis B antigen."

Then on to the next page, SNB0067633, a bit more discussion of Hepatitis B and then at the end of the first paragraph on the page:

"It was agreed that the theoretically increased risk of acquiring hepatitis, which does not seem to be borne out in practice, should not be a deterrent to using the freeze-dried preparation, and in any case, this complication will decrease with the universal screening of donors for hepatitis antigen."

I suppose one should really read implicit in that: Universal screening of donors for Hepatitis B antigen:

"At a meeting of the haemophilia centre directors in 1972, there was a consensus of opinion in favour of freeze-dried concentrate. This was confirmed in a survey undertaken by Dr Maycock of the opinions of clinicians. The limiting factors are the capacity for production and the cost of this preparation."

Then there is a marginal note that one might speculate is possibly in the handwriting of Mr Watts, but it is not really known:

"This was not communicated to PFC or SNBTA."

Looking further down the minutes of this meeting, the second last paragraph:

"At present, UK production is considerably less than the required amount of the freeze-dried preparation. It was agreed that there is an immediate need to discuss the advisability of central purchase and distribution of the two commercially produced preparations. There is also a pressing need to seek ways of increasing UK production with the intention of reducing and, as soon as possible, ending purchase from foreign sources."

Then on to the next page, 7634, third paragraph:

"Close cooperation between England, including Wales, Northern Ireland and Scotland, will be required in order to co-ordinate and optimise blood collection and transport. The fractionation process is distribution of the therapeutic agents and utilisation of other blood fraction by-products."

Then the recommendations by the expert group:

"1. There is to be early consideration of central purchase of the freeze-dried concentrate from the two firms. 2. Distribution to other haemophilia centres and hospitals should be through the regional centres, three of which are in Oxford, Manchester and Sheffield in England, one in Scotland, Edinburgh or Glasgow, and one in London."

That is to ensure the most effective use of available material:

"3. At the same time, the UK should aim to become self-sufficient as soon as possible by increasing home production of freeze-dried AHG concentrate."

Then:

"5. There should be further meetings of this expert group ... several subjects need to be discussed further, including home treatment, and, in due course, prophylactic treatment.

"6. The expert group membership might be expanded to include representatives of each of the Regional haemophilia centres, a representative of the Regional Transfusion Directors [and possibly senior administrative medical officer]. It is also suggested that the National Medical Director of the Scottish National Blood Transfusion Association a Mr Watt of the Edinburgh BPL [as it is inaccurately described -- of PFC] should be invited to join the group."

THE CHAIRMAN: Before you leave that, on the first page where there is a reference to the size of the problem and then at several points thereafter there are references to the UK, and this is of course a problem that runs through many of the documents, do we know whether the "UK", so described in this document, is

a reference to England and Wales or indeed to the United Kingdom?

MS DUNLOP: Well, given that there does appear to have been representation from Scotland, I would suspect -- I don't know is the answer to the question, sir, but I would suspect that the numbers that are given for the UK probably does include Scotland. There is some attempt made at some points in this minute to record that a particular figure relates only to England and Wales. For example in paragraph 3 when there is a discussion of cryoprecipitate. It is recorded that the figure given there is relating to England and Wales.

THE CHAIRMAN: Because the other point is that PFC hadn't been commissioned by this date.

MS DUNLOP: Yes.

THE CHAIRMAN: The first comment about the UK is just something that we have to bear in mind. I think that it becomes clear in time that in documents emanating from the DHSS there are often references to the United Kingdom which probably can only relate to England and Wales and it makes understanding quite difficult.

MS DUNLOP: Yes. I think sometimes one can derive a reasonably accurate perception from the context but, as you say, sir, there may be occasions where it is really impossible to tell.

We can then look at an SHHD letter to medical officers in Scotland, which is [SGH0029309], and see that this is dated 28 March 1973. It's actually virtually identical to the English one. If we could maybe juxtapose the two documents. So can we keep this one and look at [DHF0012122], which was the first document we looked at.

If we look at them side by side, we can see that although the order of the paragraphs has been changed, I think that's really enough to let us see that the two letters have the same beginning and then the Scottish one goes on to say:

"In view of several developments ..."

Which is paragraph 4 of the English one, and then the conclusion is reached in paragraph 5 of the English one and then the same text:

"Production of human concentrate in the UK is at present insufficient:"

Production licences recently granted to two firms. The department hope to let you have a further statement soon. Then a new paragraph in the Scottish circular, this is the last substantive paragraph:

"The longstanding arrangements under which the Scottish National Blood Transfusion Association prepares and distributes AHG and cryoglobulin precipitate for the

treatment of haemophilia will no doubt be well-known to those concerned."

That's, I think, the only difference between the two letters. Then if we move to the autumn of 1973 and we look at a DHSS circular letter again, this one is dated 23 October 1973. It is [SGH0029308]. We can see that this is narrating how events have moved on since March:

"I wrote to you on 6 March informing you of recent developments in the availability of freeze-dried human AHG concentrate. The expert group which met in March reached certain conclusions which the department are now using as the basis for planning for the future, including a recommendation that arrangements should be made for central purchase of the concentrate."

We see that:

"Supply division are negotiating with Travenol Laboratories Limited and Serological Products Limited for the supply. Details of the supply arrangements will be circulated as soon as possible. Meanwhile, the department, in close cooperation with the Scottish Home and Health Department, is considering ways of increasing NHS production."

Then we can see the Scottish equivalent is [SGH0029306], and again there is a close similarity between these two letters, although the Scottish one

contains a different paragraph, paragraph 3:

"I should like to remind you of the arrangement referred to in my letter of 28 March, whereby the SNBTA prepares and distributes AHG and cryoglobulin precipitate for the treatment of haemophilia. The department is considering ways of increasing NHS production."

So that, sir, is really just a bit of a glimpse of what was happening in 1973, what effect was produced by the news that commercial concentrates or superconcentrates had arrived, the need for the NHS to step up production, the need for control about how the commercial concentrates were purchased and distributed. These are all threads that one can detect in the communications, and perhaps arguably a slightly more optimistic prediction of the future, or slightly more optimistic spin in Scotland as to what might be possible by way of NHS production.

Moving into 1974, there was a meeting of haemophilia centre directors and blood transfusion directors on 31 January 1974. The minutes of that are [SNB0072190]. A very long list of attendees. Again some names that we certainly recognise. If we go to page 2195, we can see -- after a discussion of what kind of material is best for treatment -- at the top of

page 6, reading just at the bottom of the previous page it says:

"The meeting was asked to indicate whether anyone would in fact prefer to have cryoprecipitate if freeze-dried concentrate were freely available. It was clear that none of the those present would prefer cryoprecipitate."

So very obvious that the freeze-dried concentrates were greatly preferred, and indeed it's evident from the minutes of this meeting that commercial AHG was already in use. If we look at 2197, which is page 8 of the minutes, we can see -- this is in the middle -- some doctors were buying commercial AHG for use in home therapy. So a prompt start there.

Then there is a further document from 1974, which is [DHF0023406], it appears to have been a paper prepared for a meeting of the expert group on the treatment of haemophilia, for a meeting they would have on 11 October 1974. We can see that this paper is entitled "Optimum use of available Factor VIII", and we can link back to the minutes we have just looked at if we see that paragraph 5 records that:

"The last meeting of the Haemophilia Centre Directors was unanimous in preferring lyophilized concentrate to cryoprecipitate."

Then paragraph 6:

"Haemophilic requirements at haemophilia centres may be divided into three classes:

"1. Routine treatment of early bleeding.

"2. The provision of cover for dental extraction and routine surgery.

"3. Cover for heroic surgery and major trauma and the management of serious bleeding in patients with anti-Factor VIII antibodies."

"There is also the rightly growing requirement to provide home treatment."

If we look at the next page, DHF0023407, there is a suggestion at the top of the page that NHS freeze-dried lyophilised concentrate should be made generally available for requirement 6.2, that's cover for dental extraction and routine surgery, and will be the appropriate material to use for home treatment when more can be made available. But then paragraph 11:

"Until NHS supplies are adequate, commercial material should be used in three areas:

"1. Material of choice for cover for heroic surgery and major trauma and management of serious bleeding in the face of antibodies.

"2. As back-up supplies for requirements 6.1 and 6.2."

That was routine treatment of early bleeding and cover for dental extraction and surgery:

"3. For the immediate provision of home treatment in suitable cases who live too far from a haemophilia centre to be adequately treated there and who cannot for the same reason be supplied with cryoprecipitate from there even if they have a deep freeze, and for whom NHS lyophilised concentrate cannot yet be obtained."

Then on the last page, 3408, we can see that an attempt has been made to produce a sort of rough costing -- I suppose it is not rough but it is limited costing -- looking at haemophilia centres in the southeast Thames region. We can see that for that region, 1972 to 1973, the cost is shown, this is cost of supplying treatment for patients with haemophilia, £5,980, rising to £9,007 from 1973 to 1947, but then the half year for 1974, £4,939, but then compared to Oxford Haemophilia Centre, for the first eight and a half months of 1974 they had spent £75,747. So one gets some idea of the escalation in cost, which occurred when the commercial products became --

THE CHAIRMAN: Dr Biggs was at Oxford?

MS DUNLOP: Yes.

THE CHAIRMAN: And her clear preference was for concentrate?

MS DUNLOP: Yes.

Then we can look at an exchange relating to the provision of NHS product in Scotland. Firstly, if we look at [SNB0072254], this is Dr Howard Davies, the consultant haematologist at Edinburgh Royal Infirmary at that time, writing to Dr Cash and saying:

"I hope you remember that sufficient supplies of human intermediate Factor VIII concentrate would be available in Edinburgh in January 1975 to cover the operative needs of our haemophiliacs and to enable me to start some of them on on-demand therapy at home."

And asking:

"What's the state of play?"

We can see [SNB0072255]. This is Mr Watt, appearing to give to Dr Cash the information he needs to reply to Dr Davies:

"Re letter of December 18."

That's the one we have just looked at from Dr Davies:

"I suggested he needed to be a little patient a little longer. Production of Interate here is not yet started and will still have volume problems for some time ... suggested April likely earliest date on which estimate of regular output will be available."

Then lastly from 1974 we can look at another

circular from the DHSS. [DHF0029393]. 5009 is the one with the letterhead on but I think the one we have is 029393.

This is talking about blood products production, recording that the Blood Transfusion Service -- I think this is probably meant to be talking about England but was true really for both Scotland and England:

"We are currently unable to meet the demands of clinicians for certain preparations of human blood. Immediate need to provide more AHG concentrate ... at present, part of the demand for these blood products is being met by expensive imported material which is now marketed in this country. As the demand increases, commercial firms may consider it worth their while to establish panels of paid donors in this country in order to obtain their supplies of human blood. Such a development would constitute a most serious threat to the voluntary donor system upon which the NBTS is founded. The department therefore regards it as of the greatest importance, quite apart from the question of costs, that the NHS should become self-sufficient as soon as practicable."

Then there is a reference on the following page, 9394, paragraph 5, to the fact that clearly it would be considerably cheaper to produce these blood products

within the NHS than to buy them from commercial sources.

Next, sir, I would like to look at a letter we have already seen in the Inquiry, which is Dr Garrot Allen's letter, [SGH0046061]. I'm sorry but this is the one that's slightly sliced off on the right-hand side, but I don't think that matters for today's purposes.

We looked at this letter in the context of topic C1, but I would like to look at it bearing in mind what we have just seen in the DHSS circular about how precious the voluntary system of blood donation in the United Kingdom was seen to be. In this letter on 6 January 1975 from Dr Garrot Allan, he is writing to Dr Maycock at BPL because of information he has learned from Dr Judith Pool about the situation in the UK:

"The only place where these two components [that is Factor VIII and IX] is prepared is at Oxford. Am I correct in assuming your laboratory doesn't produce them? No doubt you also know what the practices in Glasgow are at the West of Scotland blood centre. Do they produce Factor VIII and IX? Dr Pool spent the past year at Oxford and tells me that at least one of the sources for commercial Factor VIII and IX is the Hyland Laboratories in the Los Angeles area."

Then he talks about a product from the Cutter company, Konyne for Factor IX deficiency has proved

extraordinarily hazardous, a 50 to 90 per cent rate of icteric hepatitis developing from it. About half of these proved fatal, Cutter's source of blood is 100 per cent from skid row derelicts."

He then talks about the relatively poor screening techniques for Hepatitis B and goes on to suggest in the fourth paragraph that half, if not more cases of post-transfusion hepatitis are caused by an agent other than Hepatitis A or B. Whatever this agent may be it still seems to be more frequently encountered in the lower socio-economic groups of paid and prison donors."

Then he says:

"A blood bank for these groups in the United States ..."

I suspect this is meant to be monetotropic, or a word of that nature, anyway something suggesting that blood banks attract people in need of money:

"Commercial blood banks attract these kind of donors. I would hope Great Britain would give some thought to what the purchase of Factor VIII and IX from the United States tends to do to our attempts to run a volunteer programme. Commercial blood banking perpetuates the high risk rates for hepatitis B encountered with their products and it tempts these same commercial firms to sell the residual products of these

high risk donors."

So he's wondering what the situation is in the UK and pointing out that it doesn't help the attempts in America to establish the sort of voluntary donor system that it might be thought was so precious in the United Kingdom if these commercial products are so readily marketable in the UK.

I also wanted, really for reference, to look at some statements in Parliament on this topic in 1975.

THE CHAIRMAN: Before you go to them, Professor James is pointing out to me that we should see the reference to the financial implications in context, that in the early 1970s the National Health Service generally was very strapped for cash and there was what he refers to as widespread occult rationing, for example in renal transplant and dialysis units, where the work was severely limited by restricted funds, and it took 20 years really to reverse that. So really one should see the references to cost as not particularly targeted at the supply of blood products, that it's an aspect of a wider problem. Indeed, he suggests that the lobby did extremely well to get the funding that it did.

Just a little bit of context.

MS DUNLOP: Thank you. The references I wanted to make to Hansard are [PEN0120185], firstly. It shows Mr George

Cunningham asking Dr Owen:

"What deficiencies exist in the supply of Factor VIII (cryoprecipitate) [rather confusingly] for the treatment of haemophilia and what action [she] proposes to take to deal with the problem."

And Dr Owen recording that:

"The amount of Factor VIII produced within the NHS is not sufficient. There is an immediate need to provide more human antihaemophilic globulin concentrate, now the preferred treatment for haemophilic patients. Part of the demand for concentrate is being met by imported material but this is very expensive. I believe it is vitally important that the National Health Service should become self-sufficient as soon as practicable in the production of Factor VIII, including AHG concentrate."

From the same year, February, [PEN0120186]. Mr GRO-A this is. I'm not terribly sure who he is/was, but he asked the Secretary of State for Social Services if she will now:

" ... consider making adequate supplies of Factor VIII available to the National Health Service so that it is self-sufficient in this product for the benefit of those suffering from haemophilia."

We see Dr Owen recording that £500,000 special

finance is being made available to increase the existing production. I think we know that that's an injection of capital that took place in England.

Then there is more discussion about the arrangements for purchase, discussion about the possibility of central purchase, and Dr Owen says:

"I confirm that in most cases I think it is the most desirable form of treatment but one cannot avoid the fact that this is one of the many costly treatments that are competing on priorities. The present system, whereby a doctor can persuade his local area health authority that his patient needs this form of treatment most is the best way of proceeding and not by central allocation."

Then there is more discussion of the benefits of treatment. Then lastly from Hansard [PEN0120183] Mr Madden really having another go on this topic. First of all asking how many patients suffer from haemophilia in Great Britain. Estimated to be approximately 3,000, a small proportion having regular home treatment. Mr Madden is wondering what arrangements, including the provision of money, are being made by health authorities to secure supplies of Factor VIII concentrate. What financial resources has each regional health authority for securing supplies of concentrate privately produced.

Then we can see from the bottom of the reference to the same two companies, two suppliers of product licenses for Factor VIII, annual running contracts with these firms.

Then on the following page there is another reference to the £500,000 injection and Dr Owen's belief that it is vitally important that the NHS should become self-sufficient as soon as practicable. Also from 1975 we should note that there was a WHO resolution on the utilisation and supply of human blood and blood products. This is May 1975 and it's [DHF0030764]. In the recital, the World Health Assembly is conscious of the increasing use of blood and blood products, considered information provided by the director general and what has been said by the Red Cross:

"Noting the extensive and increasing activities of private firms in trying to establish commercial blood collection and plasmapheresis projects in developing countries, expressing serious concern that such activities may interfere with efforts to establish efficient national blood transfusion services based on voluntary, non-remunerated donations."

Then:

"Urging member states to promote the development of national blood Transfusion services based on voluntary,

non-remunerated donation of blood and enact effective legislation governing the operation of blood services and take other actions to protect and promote the health of donors and recipients."

So it is very clear that the WHO view was that national blood services based on voluntary donations should be the aim of all countries.

Then lastly, just to look at a paper, which was presented at a World Federation of Haemophilia International Society of Blood Transfusion symposium in Helsinki, between 27 July 1975 and 1 August. [LIT0010150]. Just to note that at that symposium there was information about the drawbacks of the use of antihaemophilic concentrates. This is a paper by Dr Mannucci. Again, a very well-known name. For the record, this paper is actually pages 1 to 5 of the Scandinavian Journal of Haematology, volume 19, issue S30, which is dated June 1977. So it was published obviously a bit of time after the symposium, but just to note from the headnote that:

"Liver disease and thrombo-embolism are the most frequent and severe side-effects associated with the use of clotting factor concentrates in haemophiliacs."

Mention of the approach which should be taken to monitoring. Then:

"These complications do not justify withdrawal or limitation of the very effect of a life-changing use of concentrates, however, awarenesses of their recurrence and of their danger requires that specialised haemophilia centres carry out, at frequent intervals, clinical and laboratory testing of the organs to allow early detection."

There is obviously within the text more discussion. Perhaps one should just look at the conclusion, to see how the discussion is reflected. That's in LIT0010153. The reports of this symposium -- this is on the right-hand side:

"Clearly show that antihaemophilic concentrates are frequently associated with side-effects which may be of clinical relevance, however, they do not justify withdrawal or a limitations of replacement therapy, which would be accompanied by a consistent deterioration of the present pattern of life of haemophiliacs. More detailed knowledge and assessment of risk factors is likely to reduce, if not to abolish, the most frequent and severe side-effects, such as liver disease and thrombo-embolism."

With that, I am afraid, rather lengthy introduction, sir, I propose that we now watch the television programme which comes in December 1975. I propose that

we should watch the two episodes consecutively. I don't know whether we will need a break. I'm not sure whether the stenographers will need a break.

The total running time, I think, is about 50 minutes, whether it might be better given that it is ten past 11 to watch the first episode and then have a short break before we watch the second episode. I'm in your hands, if we want to watch both episodes consecutively.

THE CHAIRMAN: Let's take it stage by stage, we will watch the first and if necessary, review the situation at the end.

MS DUNLOP: The other thing I need to mention is that we have copies of a transcript of the programme. The transcript is [PEN0131400]. There are hard copies of the transcript. I would have thought it is better to watch the programme rather than sit reading the transcript but certainly if people want to take away a copy of the transcript at the end, they will be available. I think we will put them in an obvious place so that if somebody wants to help themselves to the transcript and take it home, there is no difficulty with that.

World in Action video played

(12.06 pm)

MS DUNLOP: Perhaps we could have a short break to make sure everything is up and running again.

THE CHAIRMAN: Right, we will adjourn.

(12.08 pm)

(Short break)

(12.27 pm)

MS DUNLOP: Sir, we have Dr Mark Winter with us to give evidence now.

DR MARK WINTER (sworn)

Questions by MS DUNLOP

THE CHAIRMAN: Do you have some difficulty in hearing?

A. Yes, I am registered deaf but I have NHS hearing-aids.

THE CHAIRMAN: Would you just sit down, we will try and bear that in mind.

Ms Dunlop?

MS DUNLOP: Thank you, sir.

Dr Winter, the first thing that I would like to do is take you through your CV which should come up on the screen in front of you. It is WIT0030359.

How is this for audibility? Is it all right?

A. Yes.

Q. Right, thank you.

First point to notice from your CV is that you show us your present appointment since 1983, consultant haematologist and haemophilia centre director, Kent and

Canterbury Hospital in Kent, but you are now retired. Is that correct?

A. I'm not using that word. I have moved on. I'm still very involved with teaching and training and I have a honorary contract with my trust, but since June of last year, I'm no longer working as a clinical doctor.

Q. So you don't see patients?

A. I don't see patients any more.

Q. Which presumably means you are not the centre director?

A. Correct.

Q. Right. I'm told that I should remind, Dr Winter, if you could, please, to make sure you speak into your microphone so that we can hear you.

A. Okay.

Q. Thank you.

We notice also from the first page that when your career began in the 1970s, you worked in haematology at the Middlesex in London and then at Guys, and in both positions you were a senior registrar. You amplify that a little on the next page, where you tell us under a subheading "Haematology", that you received a general introductory training in laboratory practice. You had a significant clinical commitment with particular emphasis on leukaemia. Then as part of the Middlesex hospital training scheme you actually spent six months

at Edgware hospital doing general clinical haematology and six months on secondment to the North London Blood Transfusion Service at Edgware.

We have heard of Edgware already in the Inquiry when we looked at precautions that were taken in donor selection in the 1980s. I think it was a Dr Patricia Hewitt who was there at one time, who I think was described to us as very forward-looking. Is this a particularly forward-looking blood transfusion centre, Edgware?

A. Not at the time I was there.

Q. No, right, okay.

At Guys you say you developed an interest in haemophilia and thrombosis, you introduced a home therapy programme for patients with severe haemophilia and set up a system for comprehensive care. Then in 1983 you went as consultant haematologist to Canterbury and Thanet Health Authority. First in Margate and then moving to Canterbury. In 1984 you were appointed as the designated HIV physician for the area and established a network of AIDS patient care in response to the evolving epidemic. Was that solely for patients with haemophilia who had HIV or was it all HIV patients in the area?

A. When we got the results of AIDS blood testing

in October 1984, in my centre only one of the regularly treated patients did not have HIV. So from that moment on we, as a centre, became very involved. One of the stipulations of the AIDS Control Act was there had to be a designated physician for each area for AIDS, and as I seemed to be the only doctor who knew anything of it, they suggested that I should be the nominated AIDS physician. So from that moment on I started to look after, not only haemophilia patients with AIDS but also people from all walks of life, and it turned out there was quite a large local gay community and also because we were fairly close to the channel ports, there was quite a lot of drug addiction. So in no time at all I was looking after over 100 patients with AIDS.

So they then took pity on me and appointed a colleague to do the leukaemia work. So from that moment on I really only involved myself with HIV carers and HIV physicians and haemophilia. But I suppose because of that, I was rather unlike my other haemophilia colleagues, I did a lot more HIV clinical work than they did.

Q. Yes, at the same time as being the director of the haemophilia centre?

A. Yes.

Q. Then you tell us on page 3 of your CV -- so on to the

following page, if we could, please -- that you were involved with the Haemophilia Society's campaign for recompense for those infected, and you were the nominated campaign medical contact for media and MPs.

Eventually the Macfarlane Trust was set up. What is the brief of the Macfarlane Trust? It is targeted towards a particular group. Is that correct?

A. Yes, the Macfarlane Trust was established for the support of patients with haemophilia who had been infected with HIV through use of contaminated blood products. So I guess, because of my HIV background, I became the medical officer appointed by the Department of Health to represent the Macfarlane Trust and also a parallel trust called the Eileen Trust, which was for the smaller number of people in Britain who had got HIV through blood transfusion as opposed to blood products.

Q. Yes. You do actually mention that further on in your CV, that, I think, it was in 1996 that you were nominated to serve on the Eileen Trust as well, and are you still involved with the Macfarlane Trust?

A. No, I'm no longer a trustee of either of those trusts.

Q. You describe the establishment of a comprehensive care centre, and it really looks from your description, which we can see in the paragraph beginning, "A comprehensive care programme for haemophilia has been implemented ..."

as though haemophilia, particularly for families with affected children, really reaches into almost all aspects of the family's life. Is that fair?

A. Yes, I think it is true that different centres look after patients not always in the same way, and some centres are perhaps rather more holistic than others. I think that one of the things we tried to do was to set up a centre where we could control all aspects of their health because we didn't trust what might happen if they went to any other part of the healthcare process without us being involved. So I guess it was comprehensive in that sense, that we always direct the patients to come through us so that we could then control everything so that even if the medical problem had nothing to do with the haemophilia, at least we could interact with the other teams and make sure that nothing inappropriate happened in their management.

Q. I think I was particularly struck by the sentence:

"Many families with infected children now choose to live in the area so as to be near the centre."

Did you also have contact with schools?

A. Yes -- well, firstly, when we have a child who is starting school, we would always go and visit the school and make sure that the school understood the nature of the haemophilia and set out those activities that the

child could and couldn't do, and we would provide written information as well as verbal information. This would usually be done by one of the nursing team and then we would establish processes of contact where anybody from the school could get in touch with us urgently if they had a problem. I mean, there were very particular issues about the 20 children we had with HIV. But maybe we will talk about that later in my testimony.

Q. You talk about the upgrading that took place of the centre in Canterbury in 1996, I think, and you say:

"It was the only comprehensive care centre not sited in a teaching hospital."

That presumably was a matter of some pride, that the centre had achieved that status despite not being attached to a teaching hospital?

A. I think we were using a sort of football analogy, that we were the sort of Blackpool of the premier league and shouldn't be there really. But, yes, it was quite a difficult process to go through and all very formally conducted, and it included a lot of input from patients, which was very welcome. So that was really a big step forward for the centre at that time because it then became a fully recognised comprehensive care centre.

Q. Right. You describe some other developments for which you were responsible. A home treatment diary, 1997,

perhaps a sign of the times then that it was known as the "filo factor", whereas now patients are issued with a palm pilot with particular software, and you say this system is now in use in many countries. You also mention a twinning relationship with a centre in Pakistan, and I expect we could spend quite a lot of time talking about the standards of haemophilia care in developing countries?

A. That experience is relevant in terms of asking the question: what would have happened if our British patients with haemophilia had not had the type of treatment that they did receive from the early 1970s onwards? Because the Pakistan experience mirrors obviously that of British patients before any effective treatment was introduced.

Q. Yes. And I know that you have watched the World in Action programme that we have all been watching, and certainly Mr Watt at the end of the second episode is talking about standards of haemophilia care in developing countries, in the Middle East and in Africa, and I imagine there are still tremendous inequalities around the world. Is that a reasonable comment?

A. A very significant percentage of the world's haemophilia patients still get no treatment. A very significant

number of haemophilia people in the world, because we know the incidence in each ethnic population doesn't vary we can work out that there must be many, many thousands of people with haemophilia who are undiagnosed. For instance, quite recently in Cambodia, they have had their first ever patient diagnosed. Well, as they have a population similar to if not greater than Britain, there must be at least 25,000 others somewhere.

Q. If we move to the next page, we see that you were involved in the establishment of the haemophilia alliance and that's an organisation that continues, is that correct?

A. It is. I was the founding medical chairman of the alliance, which was sort of born out of a concept, I think, firstly that there had been diversity of care given to people with haemophilia in the past, as of course happens in all aspects of medicine, and that also maybe some of the very significant problems that had occurred with haemophilia patients might have been lessened if we had had what you might call better politics.

So although there were haemophilia organisations like the UKHCDO setting up formal protocols, the concept was that it would be good to have an across the board organisation involving doctors, nurses and patients,

where we could say to politicians and commissioners, you know, we are the voice of the haemophilia community and this is what we think.

Another major aspect of the work of the alliance was that for the first time a group of us produced a national service specification. So this was a standardised document setting out the standard of care that people with haemophilia and related conditions should receive. It had the formal blessing of the Department of Health. It was published, I think, for the first time in 2001. It has recently been republished. There is a website. I like to think that it has been seen as influential because, as I say, it was saying to commissioners of healthcare, "This is the standard of care that you should be commissioning for your patients with haemophilia", and it was hoped that it was of benefit to local haematologists round Britain who could go to their own commissioners and wave this document and say, "This document is the national service specification. It says, I ought to have the following facilities and I don't and what are we going to do about it?"

THE CHAIRMAN: Dr Winter, do you know of any other group of patients with particular conditions who have got that level of influence?

A. I think the kidney doctors are very well -- there is a lot of similarity actually between haemophilia and the management of renal disorders, where it is often very long-term, very intimate relationships between doctors and nurses and patients and they also now have a kidney alliance but I think we were there first.

MS DUNLOP: Are you still involved in the alliance?

A. No.

Q. Then you talk about research. I took it from what you said earlier that you are still interested in and involved in research. Is that --

A. No, not clinical research. The work I'm doing at the moment is just involved with teaching and training. I'm not involved in any clinical activity or any research any longer.

Q. On the following page you set out some of your experience in teaching, your membership of learned societies and the administration roles that you have held. Then if we move to the next page after that, you chart national activities within haemophilia care, quite a long list, Dr Winter. We see the Macfarlane Trust and the Eileen Trust mentioned. We see that also between 1987 and 1991, you were the nominated media liaison for the compensation campaign of the Haemophilia Society, and indeed from the bottom we see that you have also

served on an UKHCDO working party on VCJD. Is that something which has also come to an end since this was written?

A. It has now come to an end, yes.

Q. Your involvement in the working party or both?

A. Both.

Q. Then you list for us your publications. It struck me you had done a lot of work with D W Jones?

A. Yes.

Q. Is that another haemophilia --

A. He is a scientist in my centre.

Q. So there are both original papers and then you list a large number of published abstracts. Perhaps you had better explain to us quite what a published abstract is and how it differs from a published article?

A. So a published article is of much more relevance in that it will have been submitted to a scientific journal and subjected to a process of peer review, and then a published abstract would not have been peer-reviewed in the same sense. It would have been part of a major scientific meeting, such as the World Federation of Haemophilia, and the meeting would have then published the abstracts in a written publication.

Q. Yes. I think we have already come across something like that when we were looking at statistics for Scotland,

and Dr Tait told us about work that the haemophilia doctors had done in Scotland about Hepatitis C, and that was by reference to an abstract. So I think we have some understanding of the concept.

I noticed from among your articles that you had -- this is number 13, we don't need to go back to it -- looked at the care and management of children with haemophilia and HIV infection and that's, I guess, a chapter in a book called "Caring for children with HIV and AIDS". Is that correct?

A. Yes, that was -- I think I was commissioned to write that because of the particular experience that we had had with children and HIV and haemophilia.

Q. You have also looked -- this is number 37 -- at the impact of HIV on mortality rates in the complete haemophilia population.

We have some statistics on that ourselves:

Your abstracts included one which caught my eye. It is number 80. I don't know if we can perhaps move on to that. Yes, it is an abstract entitled, "When supplies run dry, how do patients cope?" Did you come up with an answer?

A. That came about because in that year one of the American companies, Bayer, had their plant shut down by the FDA. So there was a transient shortage of commercial

concentrates, which lasted for a few months, and we therefore had to alter our clinical practice, mostly in terms of postponing non-essential surgery and looking at treatment regimes and maybe talking to patients on home therapy about moderating the amount -- the dosage of Factor VIII and Factor IX they might be using for self-injection. So it was a phase that lasted quite a few months and it did cause some problems at the time.

Q. Thank you, Dr Winter. With that completed, I would like now to put before the Inquiry two documents that you have provided to us. One is a written submission you made for the Archer Inquiry, which is [PEN0150283]. There is also [PEN0150292], which is a document prepared for this Inquiry and which consists of a series of answers to questions that you were sent by the Inquiry team. I'm not sure if you have hard copies with you?

A. I do.

Q. Yes. Please feel free to use those rather than watching it on the screen.

You gave evidence to the Archer Inquiry, I think, in 2007. Is that correct?

A. Yes.

Q. You make the point in your statement to the Archer Inquiry -- which I think you delivered orally in evidence at the end of the first

paragraph, that you did that in a personal capacity, not representing any of the organisations you named. That would be the UKHCDO and the Haemophilia Alliance and so on. Should we take it that that is also true today? You are here in a personal capacity and not representing any bodies?

A. If you would, please.

Q. Yes. Thank you.

The first short point, I think, perhaps we could take from you, Dr Winter, is something that's mentioned on the first page of that submission and it's the reference to "life expectancy", which without treatment, you say -- and this is near the bottom of the page, the second line under the heading "Spring 1984":

"Without treatment, we know that life expectancy is very limited."

Without going to the other paper, I think we asked you about the Birch Report, which I think was written in the 1930s but was actually an American publication. Is that correct?

A. Yes.

Q. But you, I think, clarified for us that there would be no reason to believe that the likely survival of untreated British patients would have been any different from American patients, and certainly at that time, you

say, only 20 per cent of patients with severe haemophilia could expect to live beyond 20 years. We have tried but not succeeded to obtain a copy of the actual paper but it seems that the figure was that 82 patients out of 98 died before they were 20. Without going to it, we refer to this in paragraph 3.49 of our preliminary report.

The next point I wanted to ask you about was the gradations of haemophilia. Perhaps we could at this point look at the other paper, [PEN0150292].

A. Could I just make parallel comment about the natural history, before we move on, if you don't mind?

Q. Yes, certainly.

A. I think it is helpful. I have mentioned Pakistan. I think it may be relevant to say that if you still want evidence of what happens when somebody with severe haemophilia doesn't get treated, you don't only need to look back to these retrospective studies, which were a long time ago and not many of them, you can go to one of the developing countries because the cost of concentrate is so significant there are many developing countries where, as in Pakistan, they have got very nice hospitals, experienced doctors, good nurses, they have a nuclear power, but they have no concentrate. In the centre in Islamabad, where we visited twice, there are

upward of 250 children with severe haemophilia, of which one of them lived beyond the age of 18.

So that remains the natural history of haemophilia. Without treatment, as happened to members of the Royal Family, the likely thing by far is that you will have some life-ending event of serious and spontaneous internal haemorrhage before the age of 20 or so years. That is the natural history of severe haemophilia.

THE CHAIRMAN: Dr Winter, when we visited Newcastle, we were shown photographs of boys in Africa today, showing very severe damage to joints and so on. Is the progressive natural history the same generally now, but for treatment?

A. It is. You can look at the old footage of the Tsarevich being carried round Moscow at the age of 8 and he is completely crippled and can't walk, and in Pakistan hardly any of the children we were doing clinics with, hardly any of them -- certainly none of them had normal joints and most of them were bedbound.

MS DUNLOP: Can I ask you then, please, Dr Winter, just one or two questions about the gradations of haemophilia. You have set this out for us on the other statement, which is [PEN0150292]. I think we have it in front of us.

You say:

"The various grades have been agreed by the World Federation as follows."

Under 1 "International Unit Per Decilitre" -- is that? --

A. Yes.

Q. -- of blood is severe and then 1 to 5 per decilitre would be moderate haemophilia and mild would be 5 to 50. I did actually have a look at the World Federation's website the other day and, perhaps slightly confusingly, there are references on it to mild being 5 to 30 per cent and normal being 50 per cent and above, and then at another point on the website mild is described as 5 to 40 per cent, which I suppose leaves you wondering about people that were at 45 per cent or thereabouts. At least with your definition all the categories join. But I suppose if people are at about 40 per cent, they don't have very many symptoms. Is that the explanation?

A. I'm not sure. There has been some controversy about this. I think from a clinician's point of view the really important point is that if you have a Factor VIII level of, say, about 40 and you then have surgery, you may well bleed very significantly. So I think from a clinician's point of view we feel pretty strongly that we would like the mild classification to go up to

a level of 50 because we think in the sort of range 30 to 50 people can have really pretty significant clinical problems at times of dentistry or surgery or following trauma.

Q. We have also already had some evidence from Dr Colvin, when he came to speak about one of the specific deaths that we have been asked to investigate, about fluctuation in people's levels of Factor VIII and, presumably, Factor IX as well. That's a physiological feature, is it?

A. Factor VIII is what is known as an acute phase protein. Let's just say you are a patient with haemophilia and your Factor VIII might be 20 and you then get pneumonia; it might transiently go up to 30. So there are times in life when you are ill in any way when this level might transiently increase.

The other aspect to all this is that Factor VIII assays are not necessarily the easiest test to do. So probably somebody who is told by one centre that their level is 10 and another centre it's 15 might actually be the same level, it is just the different laboratories doing the test. It is, as I say, not necessarily a very straightforward test to do and there is still quite a lot of technical discussion as to the best way to do it.

Q. Is there a danger, therefore, that these sorts of figures give an impression of precision which isn't achieved in clinical practice?
A. Yes. I think we wouldn't get too excited about a level that varied by, say, 5 IU per DL. We wouldn't be at all surprised to find that, for instance, our centre had found a level of 12 and another centre a level of 17. That would not be a surprise.
Q. What about differences between, say, 7 and 11 or 7 and 12, something that, obviously, you know, covers one of the boundaries?
A. That would be less likely. If you talk about people with severe haemophilia and they have a gene deletion so that they can't make any Factor VIII protein at all, which is a significant percentage of patients, then that Factor VIII level won't, of course, increase as an acute phase protein because even if the patient has got pneumonia, they haven't got a codable Factor VIII gene that can make any protein under any circumstances. So I think for very severely affected patients we wouldn't expect the level to change but this dynamic with the milder patients is seen from time to time, depending on how the test is done and depending on the general health of the patient. For instance, we have had patients who have developed arthritis in older age, so they have got

ongoing inflammation. Their background Factor VIII might have gone from 20 to 30.

Q. Yes. Of course, my example, 7 to 12, wasn't a good one because I was really looking for something which obviously could be within one category or the other. But does what you said also hold true for somebody whose measurement might be, say, 4 one day and then 8. You would just say that that is very unlikely?

A. I think these variations are much less likely in the severe and moderate categories.

Q. I wondered too whether the definition or the classification of a patient's haemophilia as mild, moderate or severe depends only on these sorts of levels or are there other factors, that can, as it were, put a patient into a different category?

A. It's complex. It is traditionally based on the level of the Factor VIII. Some patients are in a situation where -- the phrase we used -- "phenotype does not equal genotype", and what that means is there are some patients where they might have extremely low levels of Factor VIII and yet they would not bleed as often as you might expect, given that very low level. Some of these patients, intriguingly, it turned out that they have already acquired another gene for clotting.

So I have one patient in particular where from his

mother he has acquired a severe haemophilia gene -- we know this little boy's uncle had severe haemophilia and died of AIDS -- but from his father I have established that he has happily inherited a thrombosis gene. So the end result clinically, although he has got no Factor VIII, his father's thrombosis tendency has made his severe haemophilia bleed much less than you would expect. So clinically he behaves like a mild haemophilia patient.

I'm just making the point that you can't always tell how often somebody is going to bleed just by looking at their Factor VIII level. Of course, another much more common dynamic would be how active is the patient. We had some children who were very, very active and very sporty and they would bleed quite a lot, and yet some other children would spend their summer holidays in front of Sky Television and not do too much and they wouldn't bleed particularly often.

So I think a lot of this is related also to lifestyle activities and also particularly to how often did they bleed in the very first few years of life because that's a great determinant of subsequent bleeding, if they develop what we call a "target joint". Let's just say that by the age of three they have had two or three bleeds into one particular joint. Then

they are much more likely than other children to get bleeds later on in life.

Q. The process you are describing of a patient whose bleeding problems are not as serious as their level might suggest, does the converse hold true? Are there patients who have much more serious bleeding problems than their resting level might suggest?

A. The bleeding patterns in haemophilia are in any case complex because they are variable. Although you may read that patients get of the order of 30 or 40 bleeds a year, an absolute characteristic which any haemophilia patient will recognise is that you could go through whole weeks with no problems and you then might have a run of several bleeds over a few weeks.

A particular precipitating factor, especially in children, would be if you had a concurrent infection. So a very common clinical dynamic in a child would be a mother would bring in an eight year old boy with a bad bleed into the knee and then say, "He has been absolutely fine but he has had an ear infection for the past week." There are scientific reasons to support the idea that bleeding in haemophilia is more likely to happen if you have a concomitant infection. Again these things are complex. Rarely, in some mild patients, they can develop inhibitors, antibodies, against Factor VIII

which would then convert them into a more severely affected patient.

Q. And have these levels at which the classifications change, particularly the level of 5, which appears to be the border between moderate and mild, changed within the past few decades?

A. I don't think so particularly. I mean, clinically, we have always worked off the criteria that you have in front of you there. I mean, these things have a wider relevance too because, of course, haemophilia centres, their funding is related to the levels of severity usually of the patients that they are looking after. So this has been a matter of some interest to all the commissioning bodies because the level of payment that they would have to make to each centre would normally be in two parts. It would, firstly, be based on the number of severely affected and moderately affected patients -- I don't know whether this situation pertains in Scotland but it certainly does in England -- and then there would be a separate component related to the individual usage of coagulation factor concentrates.

This is something which has exercised the commissioning bodies quite a lot. You know, they would say to a centre, "When you say you have got 40 severely affected patients, can we be absolutely clear what

classification you are using to define the phrase 'severely affected?'" And for each severely affected patient there would be a payment of maybe £4,000/£5,000/£6,000/£7,000 a year for the clinical care that that patient received. That would exclude any cost relating to coagulation factor concentrates, which, of course, could be extremely high.

Q. So, just as an example, these considerations about how you grade someone's haemophilia, could somebody with a level of 10 international units per decilitre still be classified as having moderate haemophilia?

A. No, not if it was 10. You would be expected to call them mild. That's not to say they might not bleed a lot more often than other mildly affected patients. One of my mild patients started to be goalkeeper for the local Sunday morning football team, so he bled quite significantly for a while, not because of his -- well, because of his haemophilia but although he was only 10 IU per DL, he was obviously participating in an activity that made him a lot more likely to bleed than other mildly affected patients of the same level.

Q. I'm conscious it is after one o'clock, so just one more question, I think, on this, which is probably quite a complicated answer, I suspect, but it is rather a daft layperson's question. I think we, as lay people, can

understand that the problem, if you lack Factor VIII or Factor IX, is that your blood doesn't clot in the same way as somebody whose levels are normal, but what is it that causes the spontaneous bleeding to start, which seems to be an event before the clotting problem?

A. It's not such a daft question as you say. It's quite complicated, as you did say.

We don't know why, I think it would be true to say, haemophiliacs don't bleed more often. They have no Factor VIII, so why do they only bleed naturally 30- to 40-ish times per year? We have evidence they are more likely to bleed when they are infected. That's probably because the infection affects the way their platelets work, which is the other part of the clotting mechanism apart from clotting factors.

We have evidence that bleeding is much more common in a joint when the joint has been previously damaged. I think that this is probably the most obvious answer to your question, that actually microbleeding is probably happening the whole time in joints and muscles, which is the site of main pathology in haemophilia.

But the patient with a joint that's quite sore on a day-to-day basis because of previous bleeding and then the inflammation that follows that can't actually work out whether the minor ache in his knee is due to his

arthritis or is it due to a new bleed. Some of these episodes of bleeding will reach a greater threshold, where the bleeding is obviously very significant, but I think our suspicion is that a lot of episodes of bleeding are subclinical and attributed by the patient to the inflammation that he experiences day to day because of all the previous joint damage. Certainly if you go to an operation on somebody's joint, which I have done, and you look at it as the joint is explored through a telescope, you can see that the lining of the joint looks like mushroom risotto, for want of a better word, and that it is very bloody.

So one would expect that these joints have been damaged by bleeding early in life. The joint reacts by -- the synovium, the lining of the joint, becomes much more friable and, like fronds of sea weed, waves in the cavity of the joint and, naturally enough, that can be a focus for very, very tiny episodes of bleeding.

Obviously, if the patient then has trauma -- about half of our patients would come in and say, "I have a bleed. I know why. I banged my elbow coming down the stairs." About half of them would say, "I woke up this morning, I have a bleed and I don't know why." So these things are by no means as well understood as you might think.

THE CHAIRMAN: Ms Dunlop, I rather think the answer, comprehensive as it was, won't meet everyone's demand for information, so we should probably stop there for lunch.

Dr Winter, I have only two things I would like you to think about a little before you come back. One is the question of the percentages recognised as mild, moderate and severe. In the preliminary report we quote a range taken from a National Health Service publication website, which gives mild as between 5 and 30 per cent. You have suggested that the 50 per cent level has been recognised and used consistently for a long time. So I might like to explore that just a little. It may not be significant in the long run but one would wish to be accurate about it.

The other thing relates to the funding arrangements that you have identified. One would be surprised if National Health Service funding had been consistent in any respect over a long period of time and I would just like to find out the period by reference to which the current arrangements existed.

(1.10 pm)

(The short adjournment)

(2.00 pm)

THE CHAIRMAN: Now, Dr Winter, is there a clear and easy

answer to either of the points made? In the first place the range. It's my impression having read documents over a very long period of time that at both ends of the range there have been changes, 2 per cent I seem to remember being used as the measure of severe haemophilia early on, though 1 per cent is certainly a steady figure at the later period, and then the 30 per cent figure that we quote in a preliminary report is rather different from yours.

But what is the position?

A. I think there has been a change, as you imply. The body that would be responsible for the classification would be the International Society of Thrombosis and Haemostasis, ISTH, and my understanding is that they have classified or changed the classification down to a level of 30 for mildly affected patients.

As I pointed out, there might be some clinical arguments suggesting that that might not necessarily be wise because it might not capture all people who might bleed easily at rare times of their life, but I think that's the correct ISTH classification as I understand it, and then certainly at the other end of the scale, particularly because of all the financial implications of what you call severe haemophilia, the consensus is that the level is less than 1.

I think, because of the clinical argument, in the national service specification we included levels of up to 50 IU per DL because I recall receiving some correspondence along the lines of why weren't we following the ISTH classification, and that is the reason why, because we were concerned that we should capture the 30 to 50s to make sure that they had proper care at the rare times in their life when they might bleed.

THE CHAIRMAN: Is it entirely coincidental that you were choosing a range that would provide for the largest number of capitation fees, as it were.

A. No, the way the capitation works usually -- as I say, this is not a national system, it is just a system that was followed by an awful lot of commissioning bodies and it recommended in the national service specification -- is that 90 per cent of all the problems in the haemophilia centre clinically would be taken up with the severe and moderately affected patients.

So the usual arrangement would be that there would be two scales of charge. I stress this is just for the clinical component. And for a patient with severe or moderate haemophilia, that charge might be 5 or £6,000 a year. For a mildly affected patient, who might be in the centre only once a year and have no problems, that

set registration fee might only be a few hundred pounds. So actually the commissioning bodies were not greatly exercised as to how we classified the mild. They were extremely exercised as to how we classified the other end.

THE CHAIRMAN: Perhaps to round this off, we have noticed a very considerable increase in the number of von Willebrand patients registered over time. Is that in the same sort of category of event?

A. Von Willebrand is not necessarily an easy disease to diagnose. I'm sure it is true that we are diagnosing more mildly affected patients than we used to. The same principles apply. These patients can have problems at certain times in their lives. And that would be the clinical driver for that expansion of numbers. And I don't think it would be true to say that there was a financial driver from a centre because these patients would only have carried with them a small degree of funding.

THE CHAIRMAN: Ms Dunlop?

MS DUNLOP: Dr Winter, I wanted to ask you just a little bit about another haemophilia treatment related question and it is the difference between home therapy and prophylaxis. I think we understand in general terms that home therapy came first and that was an idea that

the patient, knowing that a bleed was coming or was happening, would be able to do something about it and then care moved on to prophylaxis. Is that right? But I thought perhaps you could say a little bit about that sequence.

A. No, it really was a major revolution when the concentrates became available, perhaps at some stage in my testimony we can talk about cryoprecipitate and the issues around cryoprecipitate treatment. But when the concentrates were introduced in the early 1970s, the major revolution that came with it is because the concentrates were so much easier to use and in particular, unlike cryoprecipitate, they did not need to be deep frozen, and in that day and age nobody had a freezer in their homes.

So Factor VIII concentrate and Factor IX concentrate opened the door for home therapy because you could issue concentrate that was small volume and that could be kept in a domestic refrigerator. So it was really from that time that the concept of comprehensive care evolved, and usually what happened was that from the age of about three, depending on the state of the child's veins and the competence of the parents, you would teach the family how to inject and the patient would go on home therapy for the rest of his life and would then come in

every two to three months, depending on the severity of the disorder, for a comprehensive clinical review.

Prior to that, schooling in particular had been so variable an experience for children with haemophilia that there was actually a dedicated boarding school in Hampshire for patients with haemophilia, called the Lord Mayor Treloar School, where many of my patients went. When the concentrate came in, the boarding aspect of that school was no longer deemed to be necessary.

So this was a very major breakthrough. It enabled patients to get control back over their lives, to be on home therapy, and in retrospect we now call this period "the golden interval". This would be sort of 1973 until we entered the years of viral contamination problems, say five or six years later.

In retrospect it seems like a golden time where here was a disease which for 2,000 years had had no treatment and then suddenly there had been this enormous quantum leap forward. People were getting decent jobs, having a decent amount of time at school, getting early treatment at home for their bleeds. That was causing less joint problems.

So everything appeared to be a major break through.

Now, the prophylaxis was really parallel with that. The practice of prophylaxis, as pioneered by the Swedish

physicians, really relates to a particular observation. If you have a child with severe haemophilia and their baseline Factor VIII level is nothing, that child will bleed spontaneously and regularly. If you have a child that is born with a level of say, 5 per cent of 5 IU per DL, that child may bleed but he will not bleed spontaneously. So the theory behind prophylaxis was if we give children regular Factor VIII, say three times a week, although it won't normalise their Factor VIII levels, it will in effect change their baseline 0 per cent into a baseline of 5 per cent so that they will not bleed spontaneously. They will still bleed if their sister kicks them but they won't bleed spontaneously. That's the basis of the widespread practice, in Europe -- it has never been very widely practised in the US until very recently -- of prophylaxis. It is the regular administration of Factor VIII or Factor IX for severely affected patients to prevent spontaneous episodes of bleeding.

Q. If we look at the 1970s for a start, the people we saw in the television programme injecting themselves at home, am I right in my understanding that that was not prophylactic treatment, that was the initial form of home therapy, that they would be injecting themselves because they had a feeling that a bleed was coming?

A. I think the prophylactic programmes didn't really get going until the 1980s because as I say, it was the Swedish experience that triggered other European doctors to get going and that wasn't really available until the 1980s.

Q. So for a person like the people in the television programme, who is giving themselves an injection because they feel a bleed is coming, I wondered if we can take joint bleeds first, does the patient just have a sensation in the joint that all is not well, and I wondered also how that is handled as between a parent and a child. How can the parent tell that the child needs an injection?

A. I think some adult patients will speak to you and the analogy would be with epilepsy. They would say there is a very early and short lasting phase of a few minutes where they have what you might call an aura that all is not well. But that would then be followed very quickly by obvious clinical signs of the bleed, wherever in the body it might be. For joint bleeding, which is the major clinical problem, it would be pain, it would be swelling, a particular feature we teach is that, because there is blood in the joint it is very hot. So we teach the families to rub the back of the hand over the affected joint and happily we have two of most joints.

So we teach them to compare the good knee with the bad knee. The bad knee will be a lot hotter. That's a very good sign of an acute episode of bleeding.

Then for children -- it is a question that the child will not be -- the child may be in distress, in particular if you passively try and move the joint. Say you have noticed that the child is limping, you are suspicious that your son might have a bleed, if you try and straighten the knee and the ankle, the child will resist because it is painful. So as well as being hot and painful to touch, he won't want you to move the joint with the bleed in it. So that's the way we teach parents how to recognise an episode of bleeding. The parents often say to us, "How on earth am I going to know?" But actually in day-to-day home life it is pretty obvious that the child does have a bleed, if it's into a joint or a muscle. It is pretty obvious.

Q. What about cerebral bleeding?

A. Cerebral bleeding these days thankfully is much, much less rare [sic] but major teaching points for families before they go on home therapy would be that there are several times when it's absolutely of the utmost importance that the centre should be contacted immediately, day or night, and that would be if the child has a significant head injury. If the child loses

consciousness, if the child starts to vomit after head injury. And then another major area would be we worry a lot about bleeding into the mouth. So these would be the big four major teaching points for families. If any of these things are happening day or night, you must get in touch right away because we would wish to administer very quick clotting factor but also to clinically assess the child.

Q. Yes. I think the point you were making was that cerebral bleed is much more rare now. Is that correct?

A. It is. Of course, for many, many years it was the leading cause of death and it does still happen but thankfully -- I guess it is because of better education and the availability of earlier treatment -- the incidence is very much less than it was say 30 years ago.

Q. Right.

THE CHAIRMAN: I think, Ms Dunlop, if we just substitute "common" for "rare" in 74/16, that will solve the problem.

MS DUNLOP: I wanted to ask you for some of your comments about the television programme. I know that you saw a bit of it again today and you have seen it at home. You have covered this in your second statement to us, if we look at [PEN0150292], and turn to page 293, you say that

you have reviewed the World in Action documentary and have the following comments. The opening scenes of various British teenage haemophiliacs. I think they were all actually from the Newcastle area. Is that right?

A. I believe so.

Q. And Newcastle was very much at the forefront of the development of home therapy in the 1970s. Is that correct?

A. It is.

Q. And that was largely due to the then centre director, Dr Jones?

A. Yes, and also the senior nurses there who were also very go ahead in the move towards home therapy.

Q. "These scenes underscore the very great improvement in quality of life afforded by the new concentrates."

Perhaps we can all remember that, I think it is the boy, Neil Robinson, who has had 98 visits to hospital in one year and three months off school. So I think we can see for ourselves that that has effected a huge change?

A. Since it is such an important point, can we just maybe walk through what it would be like to have one episode of treatment on cryoprecipitate, because this was the situation that arose in 1983 and 1984, as we shall discuss: should these children and other patients be

switched back from concentrate to cryoprecipitate? There was very significant patient opposition and Haemophilia Society opposition to any such proposal. We know -- and you have probably already heard evidence -- that although cryoprecipitate was the first ever effective treatment, it had some clinical problems attached to its usage, because firstly it was high volume. So it was difficult to give to children and difficult to inject. It was very laborious to draw up. It might take two people one hour to prepare it from about 20 frozen bags, which had to be pulled out of the deep freeze and put into a water bath to thaw and then reconstituted. You didn't know how much Factor VIII was in each bag, so you couldn't scientifically calculate a dose for the patient and it could have quite significant side effects, in terms of shakes and shivers and chills.

Added to that, let's just walk through a realistic event in the life of a patient who has a bleed and they need to come to hospital for some cryoprecipitate. There are 168 hours in a week; the haemophilia centre staff are probably there for 50. There would be a good chance that the patient would have to come out-of-hours. That would mean going to a casualty department. It would be extremely unlikely that the doctor seeing them

knew anything about haemophilia, which meant there would probably be a delay while the doctor worked out what he was supposed to do and ask. The patient would probably tell the doctor what he had to do. The doctor would ring the consultant haematologist on-call who would say, "This patient needs to have 20 bags of cryoprecipitate. It's available from the blood transfusion department, they will show you how to give it."

The doctor, when he found the time, would consult the blood transfusion department, who were also very busy because they were crossmatching blood for emergency patients and eventually the cryoprecipitate might be prepared by the doctor or by the technician.

The doctor would probably then offer to do some blood tests to see if the patient still had haemophilia, which wasn't very relevant. He would almost certainly want to keep the patient in overnight, he might want to gain venous access with a very large needle rather than the small butterfly needle which was perfectly suitable. By this stage it is probably four to six hours after the patient has arrived, and -- I have laboured this point because it was a very harrowing experience. I have never, in all my years of haemophilia, ever heard a patient say, "I went to casualty with a bleed and everything went well". It never does, for pretty

obvious reasons. These departments are very busy. The doctors know nothing about the condition, and haemophilia is rare.

So not only was cryoprecipitate not a very good medical treatment, for the patients it was a pretty dreadful experience having to go to hospital to have that treatment. So that was why, when one spoke to patients or you went to residential Haemophilia Society weekends, there was a very strong, very strongly expressed view from the patients of, "We want concentrate, not cryoprecipitate and we want it to be British concentrate, not American".

Q. Yes. Dr Winter, there are a number of different strands in that, most of which I'm hoping to pick up, but while we are on the topic of cryoprecipitate, you actually also say in paragraph 1.8 that it was associated with the chills and shakes. Which I think is a reaction you say to pre-existing antibodies to plasma proteins. So a sort of immune response. Is that correct?

A. Yes, some patients who have had multiple previous transfusions, which includes most haemophiliacs, can often react with protein impurities in the cryoprecipitate and that can make the administration of the cryoprecipitate really quite an unpleasant experience for the patient. Over the period of an hour

they might shake and shiver and run a fever and have muscle aches and feel generally unwell.

Q. In your second paragraph, at 1.5, if we can go back to that, please -- that's 0293 -- you say:

"The programme sets out visually what was already clear at the time: blood products derived from commercial donations are significantly more likely to be associated with viral infections."

I think near the beginning of the programme we are told that paid donors have six to 13 times the risk of having hepatitis, and then doctor Garrott Allen goes on to say -- and I appreciate this is a slightly different point -- that commercial concentrates have a six to 70 times greater risk of carrying hepatitis than product made from donors who are volunteers; although he goes on to say, instances of volunteers, friends and relatives, which perhaps is rather more low level than anyone was really achieving at that time.

Then in his second letter, of 13 February 1975, which we don't seem to have, he says that the attack rate -- that is the rate of people who suffer hepatitis -- is astounding. The programme seems to be talking about pools of around 12,000 donors; we can see all this from the transcript, but just to take it shortly, the programme discusses taking half a litre

from each donor and saying that the pool size at that point could go up to 6,000 litres. So we would then be talking about 12,000 individuals, obviously. But indeed the pool sizes that I have seen quoted go very much higher even than 12,000 individuals. There has been mention of pool sizes in the 20,000 and even, I think on one occasion, 30,000. So --

A. That was my understanding, that by the time concentrate production was well underway by the mid 1970s, the pool size would be at least 20,000 and sometimes higher.

Q. Yes. This is a point that we need to look at in much more detail, I think, when the Inquiry comes to look properly at the topic of Hepatitis C, but would it be correct to say that in essence you do reach a pool size where all the lots prepared from that pool will have hepatitis, and I'm talking about Hepatitis C?

A. The mathematics is actually quite straightforward. There are studies showing that the incidence of the virus that we now know as Hepatitis C in US donor plasma in the 1970s was of the order of 1 per cent. So if you were giving somebody with haemophilia a treatment that came from 20,000 donors, and one in 100 of them had Hepatitis C, each time the patient had a treatment they were getting a couple of hundred, at least, different Hepatitis C infections, and of course this treatment was

being given to them maybe 30 to 50 times a year, or even more often than that.

So our understanding, as haemophilia doctors, is that it was absolutely inevitable that if you had Factor VIII concentrate in the 1970s, particularly from US donor plasma, it was absolutely inevitable that you were getting a number of different Hepatitis C infections, and clinically quite an interesting observation that has been made is Hepatitis C comes in different genotypes, six different genotypes -- I say quite often, there have been quite a few experiences in my centre and in a number of other centres that we have treated a patient with a known genotype, say genotype number 1, and we have cleared that genotype and retested him to be then told by the viral laboratory we have now found another genotype. So our understanding based on this mathematics is that these patients were multiply infected with Hepatitis C, as we now call it.

THE CHAIRMAN: Does the arithmetic go even further? If you are taking 20 bags out of the freezer, I suppose it is unlikely that the constituents contributing to each of those bags would be the same.

A. Yes, that was the difference in risk, it was 1 in 20 rather than the other...

THE CHAIRMAN: Yes.

MS DUNLOP: There were certain points made in the programme about what we might call the donor constituency shown in some of the blood centres, in particular alcohol consumption, malnutrition among the donors.

I understand that that is relevant to whether the donor should be giving blood at all, but is that relevant to the recipient, somebody receiving blood products made from blood donated or plasma donated by those donors?

A. Not in terms of the quality of the Factor VIII that would be in the eventual batch. That would be unaffected by those health issues. Obviously, the major consideration was the viral status of any donors, but whether the donor was underweight or drank alcohol would be of less significance.

Q. In fact a bit of a red herring, the references to alcohol and the pictures of people with bottles sticking out of their pockets, maybe.

There also perhaps was a bit of the blurring of the edges, understandably, given that it was 1975, but at one point hepatitis is spoken of as an illness that can make you seriously ill with jaundice or chronically ill or something that you can get from insanitary conditions. Is that a bit of a blurring of the different types of hepatitis?

A. I felt -- I had seen the World in Action documentary

some years ago, but looking at it again recently, Professor Zuckerman and the others really are talking about Hepatitis B. So let's be clear.

In the mid 1970s -- let's just say concentrate had been in use for two to three years -- many patients with haemophilia were displaying blood tests suggestive of a hepatitis-like pattern in their liver function blood tests. They were, by and large, very well. It was possible to demonstrate that maybe 5 per cent, perhaps slightly higher than that, had circulating levels of Hepatitis B; a small per cent could be demonstrated to have Hepatitis A, so-called infectious hepatitis; about 20 per cent could be shown to have antibodies against Hepatitis B and had therefore been exposed to Hepatitis B, but for the majority of these other patients, who clearly had a hepatitis-like picture on their liver function blood tests, all the standard Hepatitis A and B markers were negative.

So it was for this reason that haemophilia doctors started to use this phrase "non-A non-B hepatitis," the implication being these clinicians were saying, "It looks to us, even though the patients are well, as if they have a third type of hepatitis, which we will call 'non-A, non-B'." When you get non-A non-B hepatitis, you can become clinically unwell but it is not

necessarily a very common event, it is not as common as having Hepatitis A or B when you normally feel thoroughly unwell at the time of the infection.

One of the features of non-A non-B hepatitis is that it only quite unusually gives you clinical symptoms at the time of the infection. It is just more likely to get into the blood stream and inflame the liver, and that indeed is what happened to the majority of the patients.

So I think it is striking in the documentary that they are really not talking about non-A non-B, but if you like, they should have because it is by far the most relevant type of hepatitis for these patients.

Q. Yes, and we will come on in a moment to look at some of the articles that we asked you to consider from the 1970s, but just to stay with your paragraph 1.5, I noted also what you had said, that:

"The practice of blood collection from developing countries, such as Africa, was always denied by the commercial manufacturers but there was subsequent evidence from the study of Hepatitis C genotypes that suggested that blood of African origin may have found its way into pools."

I just wanted to show you, and to show the Inquiry, another extract from Douglas Starr's book. It is

page 233, which is [LIT0012901] at 2903. By way of illustration of the point made about plasma from the Third World, he discusses the centre that used to exist in Haiti. By the beginning of the 1970s, a likely trade was already underway. The first centre to receive public attention was a facility in Haiti called Hemo-Caribbean, the most impoverished capital in the western hemisphere, Port Au Prince, and it discusses the mechanics of how the plasma was collected and taken for fractionation; about the payments, $3 a litre or about three times the average daily wage, but the condition of the donors was deplorable.

In fact, we see, if we go a little bit further down the page, what happened to that particular one was that Baby Doc Duvalier was stung by some of the criticism, and after only 22 months of the centre's 10-year contract, he closed Hemo-Caribbean. So it would seem, as you say, there is indirect evidence by way of the genotypes that have been found but there is direct information as well about there having been plasma collection centres in Third World or developing country locations.

You presumably knew that there had been this facility in Haiti?

A. I was aware of the Haitian facility and that the biggest

plasmapheresis plant in the world was in Nicaragua.
Q. Yes, which is also discussed in the Douglas Starr book.
A. There is data about Hepatitis C genotypes. We started to talk about matters haepatological, on which I'm not an expert.
Q. We are going to have quite a lot of evidence about that in the autumn.
A. Okay, but let me, if you wish, just say that my understanding is that Hepatitis C comes in six genotypes. Genotypes 1, 2 and 3, are usually found in European and American peoples. 4, 5 and 6 are more often from the developing world, particularly Africa, and a paper was published by the group of Professor Eric Preston in Sheffield on a quite large number of patients with haemophilia, more than 100, showing that quite a significant number of those patients, their Hepatitis C was of genotypes 4, 5 or 6, the implication being that that virus might have come from donors who lived in Africa rather than America.
Q. Yes. Just before we leave the programme, Dr Winter, the whole programme, in fact both the programmes, are interesting but I wanted just to highlight a few of the comments made. If we could look at the transcript, [PEN0131400], and if we could go to the second page, so 1402, thank you. What Professor Zuckerman says there:

"Hepatitis or jaundice is a particularly interesting infection because the severity of the illness ranges from a very mild form of infection, perhaps with trivial symptoms, to an attack of jaundice with quite a lot of disability which may last for some weeks or perhaps even months, and is associated with a significant death rate. In addition, in a number of cases it may progress to chronic liver danger and may end up in a condition such as chronic active hepatitis or cirrhosis of the liver."

In essence what he is saying in that paragraph beginning "in addition", is really non-A, non-B or Hepatitis C?

A. It is, yes.

Q. So perhaps, unsurprisingly given his expertise, that seemed to me to be spot-on; is that reasonable, what he is saying there?

A. Yes, I think it mirrors the comments I have just been making to you, that the clinical presentations of viral hepatitis of whatever type are variable, and that can often -- particularly with non-A non-B -- go on to chronic illness which eventually, after a good many years, can be very significant in terms of damaging the health of the patient.

Q. Yes. Then if we could look at -- I think it will be 1409, please -- Dr Garrott Allen. Unfortunately I have

a copy which is numbered -- I'm not even sure that it is paginated in the same way.

Could we go two pages before that, please? Yes, that answer that's just at the foot of the screen, where Dr Garrott Allen says:

"We really don't know how many viruses are involved. There are at least two and perhaps more. The major one, Hepatitis B, is detected fairly well. It appears that at least two-thirds more infectious bloods or donors will escape detection by the use of this test because the test does not apply to their virus."

I think it follows from everything you have said that that's spot-on as well?

A. Absolutely correct.

Q. Then Dr Mosely on the next page, he says -- it is that answer there, beginning "well" that I'm interested in. Dr Moseley is asked about the chances of catching hepatitis from using a product made from the plasma of these type of people, and Dr Mosely says:

"If it is a blood product that cannot be sterilised..."

This is Dr Mosely of UCLA:

"... that is true for the clotting factor concentrate; it can't be sterilised. The risk is probably 100 per cent if the individual is susceptible."

I'm not sure quite what he means by "susceptible". Does that mean: doesn't have antibodies?

A. I think so, yes.

Q. So for somebody who doesn't have antibodies, the risk of getting hepatitis from a clotting factor concentrate is probably 100 per cent. That was accurate as well, was it?

A. Well, it mirrors the comments I have made to you a few minutes ago.

Q. Yes. Then lastly I wanted to look at what was said by one of the commentators from the Haemophilia Society. I think you recognised some of the people in the programme, Dr Winter, is that right?

A. I did. It was very poignant really because I knew some of those people who had haemophilia and it was very poignant to see them discussing whether these viruses had any relevance to them which, of course, in due course they did.

Q. A particular comment I wanted to look at is from committee member number 4 and it's on 0131418. Really quite a considered comment from someone thinking about the different dilemmas saying:

"One of the things I noticed on that programme was the sort of ethical problems and social problems which it posed, and that's the question whether the less

fortunate people should be used, or used as donors. Whether we should take blood from them; whether commercial firms should take blood from them. And I'm quite sure that the answer for the haemophiliac in this country would be: he is not really too bothered about where the blood comes from as long as he has that blood concentrate to keep him going, and in some cases to keep him alive. No doubt whatsoever in my mind. Of course, he would much sooner, if there were sufficient number of well disposed people, thousands upon thousands of them already in this country would come along and regularly and give blood, who weren't undernourished and weren't alcoholics, I am sure they would be delighted."

Does that really encapsulate an attitude you recognise as well?

A. I do recognise that. I mean, in my centre, for various reasons, the supply of NHS concentrate was extremely limited. I would think at least 90 per cent of the concentrate we used was commercial in origin, and in all our interactions with the Regional Blood Transfusion Service and with the BPL plant at Elstree, I had always understood that the limiting factor in the production of NHS concentrate was not related to the number of donors. The problem was the capacity of the plant to produce the clotting factor concentrate. So, if you like, you know,

there was not a particular issue about there being enough blood donors. That was not the limiting factor as to why there was not more NHS-produced concentrate available at that time. It was to do with the capacity at Elstree.

Q. I suppose too the committee member is saying that the bottom line perhaps, particularly for someone severely affected by haemophilia, is that this product makes such a huge difference to his life that these considerations about source and so on took second place?

A. We heard on the video, even the man who said, "I have actually been sick with this concentrate because I have hepatitis, but I'm still going to go on with it". That's a mirror of, as I have been trying to reflect in my comments, the quite extraordinary change of quality of life for these people whose existence had really been pretty miserable, regular bleeding into joints and muscles, poor schooling, lifelong pain, no sport, limited ability to get jobs because of poor education, and suddenly there was this white powder they could give at home and it had an enormous difference. So for all these reasons, when faced with this variable data with variable opinions by doctors, their view was, "Well, we are extremely reluctant to consider not using this product any more because of the quality of life it has

given us".

Q. The Inquiry team did try standing what's said in the programme about hepatitis in the mid 1970s, associated with concentrates -- we did try to find some articles that might reflect that outbreak and we did, I think, send you three of those articles and I would like just quickly to look at them really in passing. The first is [PEN0150238]. This is from the Lancet of 2 August 1975. I think somebody at some point has highlighted this but we can probably just about read it:

"An outbreak of hepatitis associated with intravenous injection of Factor VIII concentrate."

We can see that the first named doctor is Dr Craske. I think we learned from the programme, although some of us had discovered this before, that he was a virologist. Is that correct? We saw him in fact in the programme.

A. Yes, Dr John Craske was exclusively really the source of virological advice to haemophilia doctors in the early 1980s, when the HIV epidemic was just getting going. He came to all our meetings, he wrote to us regularly and it was more or less exclusively him that we derived all our virological advice from.

Q. Yes, and really this article is making the same points that we have just been discussing and that were in the programme, he says in his summary and the authors say in

their summary:

"An outbreak of jaundice associated with three out of four batches of a commercial brand of freeze-dried Factor VIII occurred at the Bournemouth Haemophilia Centre in 1974. Seven cases of non-B hepatitis, four of Hepatitis B."

Then in the introduction the point is made about the huge improvement brought by concentrate treatment:

"They do not produce pyrexia and urticaria which occasionally occur with cryoprecipitate."

That will be the chills and shakes, will it?

A. Yes.

Q. And then:

"Commercial Factor VIII concentrates ..."

Looking at the next paragraph:

"... prepared from pools of 2 to 6,000 litres of plasma can be expected to carry a much higher risk of transfusion hepatitis."

And they go on to say that's what they are reporting.

There is a much more detailed description of the outbreak and of the tests that were carried out. Just to look at the passage at the end of the paper, if we can look at what will be page 0240, two pages on, and highlight perhaps what he is saying in that paragraph:

"There seems to be a pronounced increase in the risk of post-transfusion hepatitis when some batches of commercial freeze-dried Factor VIII concentrates are used. This must be balanced against the undoubted advantage that freeze-dried product has over cryoprecipitate."

I don't think we have any difficulty in understanding, Dr Winter, that this is all about balance. Then there are some measures suggested:

"1. Commercial Factor VIII concentrates should be reserved for the treatment of life-threatening bleeds in all haemophiliacs and for covering major operations."

That wasn't really what happened, was it? That recommendation is pitched more highly than was actually put into effect in the 1970s.

A. No. By the way I didn't hear you clearly. Urticaria is a nettle rash and not shakes and shivers. It is part of the side effects that people can get with cryoprecipitate.

Q. Pyrexia and Urticaria.

A. Urticaria is a nettle rash.

Yes, the first recommendation there is not feasible because there was not enough NHS concentrate to sustain the requirements of the haemophilia population in either -- in England. So it would not have been

feasible to have followed that recommendation.

Q. The second one, although it is not explicitly expressed in this manner, reads as though it is meant to be a sort of fallback, I think:

"If used for treatment, commercial concentrates should be reserved for severely affected haemophiliacs."

A. But the second recommendation is, in any case, not relevant because the major hepatitis we now know is Hepatitis C, so the fact that the more severely treated patients might be immune to Hepatitis A or B wouldn't actually be relevant.

Q. I suppose it is a bit of a contorted logic --

A. The paper generally states exactly what you would expect. If you give Factor VIII concentrate to patients with haemophilia at that time, they nearly all get abnormal liver function tests, yet only a minority of them get clinical symptoms. That's exactly what you would expect.

Q. I suppose if you decouple his rationale, since they are more likely to be immune to Hepatitis A and B, and just treated the recommendation on its own, if used for treatment, commercial concentrates should be reserved for severely affected haemophiliacs, at least in the beginning when NHS concentrates were still being made from quite small pools, that might have protected,

I suppose, some of the less severely affected haemophiliacs from non-A non-B.

A. Well, in due course there were still -- it came to pass that NHS concentrate did transmit Hepatitis C, as you will be aware, so it wasn't really a safer option.

Q. In general terms, though, he is urging caution and the pattern of that seems to continue with a letter in the Lancet two weeks later. This is [PEN0150241]. This is the Lancet of 16 August 1975. This is from Dr Dane and Dr Cameron at the Middlesex. You presumably recognise these names too. Did you work with doctors Dane and Cameron?

A. Indirectly. They were in the department above mine. Dr Dane was a very distinguished virologist, in fact the core of the Hepatitis B virus is known as the Dane Particle discovered by him. So he was a very distinguished virologist at the time.

Q. It looks that in this letter, the point that's being made is about an improvement that could be brought about by a different form of screening. Looking at the paragraph beginning "during the past year," it looks as though what they are saying is that the manufacturers had been using CEP for screening donations and RIA for testing the final product. The RIA testing contributed little to safety because of the dilution factor involved

in a large pool product. They are advocating that the actual donations themselves should be screened by RIA.

A. So this discussion is all about Hepatitis B.

Q. Yes.

A. This is a discussion about different ways of testing for Hepatitis B.

Q. In a sense, doctor, this is leading people in the wrong direction because it is creating a kind of reassurance, "Well, if we can just do something about better screening for Hepatitis B, we will solve the problem," but history was to reveal that actually there was another problem of a different nature.

A. Yes. It turned out that Hepatitis B was a relatively minor problem in relation to hepatitis viruses transmitted by pooled coagulation factor concentrates. Hepatitis C was a much greater problem. About 3,000 people have Hepatitis C in this country from treatment of their haemophilia.

Q. Yes. The third article I wanted to look at is [PEN0150228]. This is back to Dr Craske, "Commercial Factor VIII associated hepatitis, 1974 to 1975, in the United Kingdom, a retrospective survey."

A paper that has been completed by September 1977. Dr Craske is saying really quite clearly, if we look just at the summary two types of hepatitis were

observed, Hepatitis B and non-B hepatitis, the latter with an incubation period of between 8 and 60 days. And we can see in fact that this is referring back to Bournemouth. It would appear that having recorded the Bournemouth outbreak in 1974 -- and there is a reference, if we go a little bit further down -- we can see that reference to Craske, Dilling and Stern. That was the first paper we looked at and he says that they went on and conducted a retrospective survey of the use of this product in British haemophilia centres.

So they really widened the net to look to see what the incidence of hepatitis was elsewhere. That is the data that they then used and they produce a table on the third page, if we go to 329, and we can see that the total number of patients transfused -- and this is in the summer as well -- was 371, and the number of patients who had one or more attacks of hepatitis was 66. And the breakdown seems to have been 48 non-B and 30 Hepatitis B. Is it possible that the non-B is a bit of an underestimate, in that the non-B may have been completely silent in some patients?

A. That would be my main comment, that I'm surprised that the non-B figure is not higher.

Q. We see a rather different classification of haemophilia here, the serious or mild.

A. Yes.

MS DUNLOP: The 2 per cent, yes.

THE CHAIRMAN: 2 per cent.

MS DUNLOP: Then in the conclusions they recite the findings, and this is page 334, so --

THE CHAIRMAN: Before we leave that altogether, is there any significance in the note that is below the table, which refers to the total number of attacks of hepatitis.

PROFESSOR JAMES: I think I can answer that actually.

They were really only recording what might be called reported cases there. So this was not, as we subsequently see, surveys in which patients had liver blood tests systematically recorded after transfusion or after some particular treatment.

So this is just a round-robin really to the haemophilia centres, and we are seeing the sort of, if you like, dying days of susceptibility of haemophiliacs still to acute attacks of Hepatitis B, when not all of them had previously been infected with Hepatitis B on the one hand, and the products were still not, as they would be a year or two later, really well screened with the most up-to-date tests. And as far as what we now know as non-A non-B is concerned, you have an "attack rate" of about 10 per cent or 15 per cent, which means of this "non-B". That means that 48 or whatever have

had actually an overt illness of some sort with abnormal blood tests. But the odds are, I think -- probably Dr Winter would agree -- that as many as another 100 or maybe even more, if you had formally tested their blood tests, would have shown a rise in the transaminase, which we now know would have been an attack of non-A non-B.

I don't know if you would agree with that, Dr Winter.

A. I would. It would be surprising if any of these patients proved not to have Hepatitis C.

PROFESSOR JAMES: Precisely.

MS DUNLOP: If we look at the entry criteria, as it were, that really makes it clear. If we go back to 229, which is page 328 in the article, it does say:

"Only patients with symptoms and signs compatible with the diagnosis of hepatitis were included. A patient was considered to be suffering from hepatitis when three or more symptoms or signs compatible with a diagnosis of hepatitis were present as indicated on the sickness record form."

So there has to have been something recognised as an illness and then evidence of abnormal liver function tests. So all these people whose liver function may have been disturbed but who didn't seem to be ill will

have been missed.

Then to go back to the conclusions, page 335, which will be 0236, he does say, particularly in paragraph 5:

"We do not yet know the nature of the non-B hepatitis we have described. The epidemiology of the disease, the definite incubation periods observed, the association with commercial plasma derivatives and the absence of illness when a convalescent patient is transfused with batches producing hepatitis in other patients -- suggesting the acquisition of specific immunity -- are all consistent with the view that an infective agent is involved, and elicits specific immunity."

There is a great deal of other material from this period, Dr Winter, but it is fair to say, isn't it, that awareness of non-A non-B really grew in the second half of the 1970s and particularly in association with blood product concentrates?

A. I think it was very well established by 1975, the group in Milan of Professor Mannucci had actually done liver biopsy studies which had demonstrated histological hepatitis in these patients as well, and it was for that reason by, you know, the mid 1970s that UKHCDO were starting to approach DOH with a view to persuading them to initiate moves towards self-sufficiency. It was the

hepatitis argument that was obviously driving this initiative.

Q. Yes. We also asked you to look at a letter which Professor Cash sent after the television programme. Perhaps we can look at that now. That's [LIT0010245]. This is the British Medical Journal of 24 January 1976, and we can see that Professor Cash firstly is making the point that journalists may take comments out of context, put them together to make a programme and create a misleading impression. He says this probably arose during the ITN television series, World in Action:

"Two consecutive programmes attempted to deal with the availability of Factor VIII concentrates."

Then he says:

"There is no doubt the import of concentrates derived from external sources represents an unequivocal pathway by which the level of a potentially lethal virus into the whole community is being deliberately increased."

That's really mainly talking about Hepatitis B again, isn't it?

A. I assume so. I don't know why he says it was deliberately increased.

Q. Perhaps "knowingly" might have been a better word?

A. Yes.

Q. Then he says:

"The absolute magnitude of the problem was exaggerated and overdramatised by the television programmes. Nobody with direct or indirect responsibility would wish to belittle the serious nature of the moral and practical dilemmas which face us all."

Then he goes on to say that:

"The other misleading feature was that £500,000 was going to fix the problem as far as domestic production was concerned."

He was right about that, was he not?

A. He was. I mean, he doesn't seem to have been right about his claim that the magnitude of the problem was being exaggerated because of the scale of Hepatitis C infection that eventually occurred in people with haemophilia that was happening at the time, but he does seem to be right about the timescale for introducing self-sufficiency.

Q. Yes. Again, like almost everything we look at, Dr Winter, it is quite complicated because if you analyse the programme as only talking about the Hepatitis B risk, then the absolute magnitude of the problem might not have been that great, but if you bear in mind that actually what was going on was that there was another hepatitis virus as well, then I understand

your comment, that actually the magnitude of the problem was not being exaggerated because there was a very serious problem developing. Is that a reasonable way of putting it?

A. It is. I mean, understandably because the virus hadn't then been identified, World in Action is really concentrating on Hepatitis B, which wasn't the major clinical problem we now know.

Q. You referred, in discussions before today, to a sort of "Tarzanoid" philosophy which operated around concentrates in this period. I think perhaps you just need to explain that for us.

A. One of the things that haemophilia doctors do is we go and run these residential weekends for people with haemophilia all over the country and you would sit down with a group of haemophilia patients from all over the UK and discuss things like this on a Saturday afternoon. And at that time the patients would say to you very strongly and understandably, as I have already recounted, that they were very strongly in favour of the use of concentrates; concentrate compared with the cryoprecipitate offered very significant improvements in their quality of life and they certainly didn't want to contemplate not using concentrates.

But then very quickly, and again equally

understandably, they would say to you they really did not want to have any concentrate of American origin. They wanted, as the patients in the World in Action documentary said, to have Factor VIII that was of British origin because of the perception, obviously enough, that British donors were voluntary donors and were therefore acting from motives that were altruistic, whereas commercial donors were doing it for money and reasons financial and were more likely to be infected with viruses.

So that was a fairly clearcut and, if you like, simplistic argument but it was very strong within the haemophilia community. In my centre, as I have said to you, we had great difficulty in getting supplies of NHS concentrate. So it took us quite a lot of work to persuade patients in some cases to continue to receive commercial concentrate because of this same perception.

Q. I think where Tarzan came into it is that it is just a very succinct way of putting it: UK good, US bad.

A. That was exactly it, yes.

Q. Yes. You said in your statement for the Archer Inquiry and this is looking at page 2 of [PEN0150283] -- just picking up this point, slightly more than half way down the page:

"A number of patients would refuse to receive

concentrate that was of US origin. It was for this reason that representation made by the haemophilia community to the DOH that there should be self-sufficiency in blood products."

I think, Dr Winter, before you arrived this morning, we also saw a lot of material from the DHSS in 1973 that would certainly suggest that the government was very concerned about cost too. It made economic sense really to promote self-sufficiency, didn't it?

A. Yes, and we heard Dr Owen's comments on the documentary too.

Q. Yes, about the pricing structures and so on. Does it really follow from everything you are saying, Dr Winter, that there was a widespread awareness among patients who were taking American concentrates, at least in the 1970s, that there were dangers of hepatitis or risks of hepatitis, or was people's understanding not as developed as that?

A. Yes, my impression was that there was widespread awareness. It was a matter that was widely discussed with the haemophilia patients. It was widely written about in the Haemophilia Society bulletin. These patients would have been tested for Hepatitis A and B. They would have been vaccinated against Hepatitis B, if appropriate. So their doctors would certainly have been

talking to them about hepatitis and the possibilities of hepatitis from concentrates. This conversation, I suspect, would mainly have been in relation to Hepatitis A and B because of the uncertain theories about the non-A non-B hepatitis, but it was certainly a topic the patients in my experience were very familiar with.

Q. Dr Winter, a slight change of tack. I wanted to take you more into the period of which you have direct experience, which is the 1980s. We can see that you begin to discuss that in the part of your statement that we still have in front of us about what happened in the summer of 1982. Just to ask you, though, about the first report of a patient with AIDS in the UK, which I think is [LIT0012479] in paragraph 8.8. If we read down, we can see that the Lancet of 12 December 1981 published a letter -- sorry, the same edition also carried a letter from physicians at the Brompton Hospital in London, the Royal National Hospital in Bournemouth, detailing the case of a 49-year old man who had reported et cetera with symptoms of, as it turned out, what later became known as AIDS.

I just wondered, you were working in London I think at the time, did you have any understanding or awareness of that happening in 1981?

A. I did. As you say, I was a senior registrar at Guys Hospital and I remember clearly the events that happened after the publication of that article because it seemed to be such an extraordinary event. It did seem to be genuinely a new disease, and I do recall that for probably at least a year or maybe slightly less than that, the major theory that was being proposed was that it was due to lack of immune function in this group of gay patients, and there was a whole series of speculations as to why gay patients might get this new disease because of an immune system that wasn't working properly. There was a lot of talk about lifestyle, agents they might be using, about poppers and things they took for stimulation, and these agents had been shown in vitro to depress immune function.

So that was for quite a time the most prevalent theory, viral aetiology was less favoured at that time, although it was noted there were some similarities between the outbreak and also the pattern of hepatitis infections. Obviously all that changed in due course when the first haemophilia patients and blood product and blood transfusion patients were described.

Q. Yes, and that, as you say in your statement, is the summer of 1982, and I think we could just quickly look at [LIT0010559]. This is a page from the MMWR,

published by the American Centres for Disease Control, 16 July 1982, and this, I think, is the reference that you are thinking of in your statement when you say in the summer of 1982, three patients in fact here are described, three patients with haemophilia A and without other underlying disease. This is still in the very first paragraph:

"All three were heterosexual males. None had a history of intravenous drug abuse."

We need to note that because we will come back to it. And at that point they were all males and two in fact had died.

Can we go to the second page, please? We can see that records of administration of Factor VIII concentrate have been reviewed:

"No two of the patients are known to have received concentrates from the same lots."

Then the editors note, if we go a little bit further down:

"Pneumocystis carinii pneumonia, not previously reported among haemophilia patients ..."

In fact we can see that this has been noted by the CDC because doctors were requesting a particular drug. Is that correct?

A. It is. This is quite an extraordinary story.

A Dr Bruce Evatt, working for the CDC in Atlanta, noticed that he was being requested for pentamidine for treatment of pneumocystis by haemophilia centres. For reasons that I'm not clear, the only way you could get pentamidine, the treatment for this opportunistic chest infection was from the CDC. There was no other outlet. And Dr Evatt noted that he had had three requests from haemophilia centres and he couldn't understand this. So he started to investigate and he was really the doctor who in 1982 identified these haemophilia patients with what became known as AIDS.

Q. Yes. And in fact we can see that's said in the second paragraph of the editorial note:

"Although the cause of the severe immune dysfunction is unknown, the occurrence among the three haemophiliac cases suggests the possible transmission of an agent through blood products."

And you are explaining to us that this is a deduction for which Dr Bruce Evatt is responsible.

Then can we go back to the preliminary report, please, and look at paragraph 8.13, which, in the report is page 189, which will be [LIT0012479]. Just after that reference, 16 July 1982, paragraph 8.13. That same month the BMJ of 3 July 1982 had had an article, "Severe acquired immuno-deficiency in European homosexual men,"

describing the cases of four Danish men who had developed KS or opportunistic infections. Three had never been to the USA.

So in a nutshell, Dr Winter, by July 1982 two things can really be said, can they, firstly it was evident that the syndrome was occurring outside the United States and secondly it was evident that people who were not homosexual appeared to be suffering from the syndrome as well?

A. That's right. Prior to July 1982 the disorder was known as GRID, Gay Related Immuno-Deficiency, and it was these reports of July 1982 that really changed the favoured aetiological agent, obviously enough towards a virus. The fact that here were this small number of patients with a blood disorder, treated regularly with blood products, here were they with the same disorder, that made viral aetiology very much more likely than the previously favoured theories, and then obviously we only had to wait a few more months before there was much clearer evidence that it was likely to be a viral disorder even though the virus had not at that time been identified.

Q. The DHSS didn't miss the point either, I don't think, Dr Winter, at this stage. If we look at [DHF0016744]. I'm sorry, I can't remember if we sent you this or not,

we have had so many documents circulating. Do you recognise this memo which is an internal DHSS memo dated also 16 July 1982? Have you seen that?

A. I haven't seen this previously.

Q. Right. I'll give you a minute --

THE CHAIRMAN: Should we take the opportunity of a short break at that point?

MS DUNLOP: Yes, sorry.

THE CHAIRMAN: Dr Winter can read it.

(3.20 pm)

(Short break)

(3.35 pm)

THE CHAIRMAN: Yes, Ms Dunlop.

MS DUNLOP: Thank you.

Yes, Dr Winter, we were just looking at this memo and actually I think it is possible to work out who wrote it because, as those who have been here before will know, we have a sort of key on one of the DOH memos that has a whole lot of names and room numbers and so on on it. But anyway I think this person is described by the DOH as a middle ranking official and he has written this, I suspect, to someone in the Department of Health, who is medically qualified, but if you look at the middle paragraph, obviously some of it is a bit flakey but given all the debate that is destined to happen

within the DHSS and so on after this, about what is or isn't causing AIDS and whether there is a connection with commercial concentrates and so on, actually it doesn't seem too bad, does it, Dr Winter?

A. I'm not sure. I don't think saying that you can look at whether somebody has injection marks or not to see whether they might be a risky donor is a valid statement, really.

Q. I think I was really just meaning, where the second paragraph records what the problem is thought to be, the problem seems to be thought to be that plasma has a sort of virus, which, when used for Factor VIII, really poses a risk to people with haemophilia; that's a reasonable sort of understanding of the nature of the problem, is it not?

A. It is in a way. I think, you know, the letter might have shown a bit more concern about it. It doesn't seem to give it the sort of importance that in retrospect we can give it. It doesn't seem to, you know, reflect that it might turn out to be a major healthcare problem, which it did. But I agree, there is nothing in it which is strictly inaccurate.

Q. Yes. I think I was just interested in exploring with you whether it shows really quite an early appreciation within the Department of Health of, in very broad terms,

the nature of the risk. I take your point that, in terms of the response, the response seems to be to move, in the third paragraph, straight to a sort of defensive position; indeed, that's the word that's used:

"We can defend the National Blood Transfusion Service's own record."

A. I mean, it does rather read as if the concern is more about the furore rather than the plight of the people in Britain with haemophilia who might have been similarly infected perhaps. Can I ask you what the date of this letter is?

Q. This is also 16 July 1982, so the same date as the MMWR report in fact.

A. So this is very early on and I agree, he or she has done well to make reasonably sensible statements, given the very early stage of the epidemic.

Q. And in fact in the third paragraph it's also recorded that about half the Factor VIII bought from commercial companies is imported from the USA:

"Your division ... "

I'm not sure quite what division this is going to, but anyway:

"Your division -- I understand one of your sections scans the technical literature for such material -- may have to consider revoking licences of certain

manufacturers. Of course, it may turn out none of the Factor VIII involved is supplied to this country."

Now, having looked at that, I wanted to go next to the UKHCDO meeting on 13 September 1982. Can you, just briefly, Dr Winter, give us a little bit of an explanation of what these gatherings were like? They are described as meetings but they are very big gatherings. They read in a way a bit like a conference. What was the general format?

A. There were two different types of meeting. There are in Britain somewhere in the order of 100 hospitals that carry the designation "haemophilia centres", and all of those centres would be invited to send a representative, usually the director, to the annual general meeting of the Haemophilia Directors' Organisation. However, of those 100 centres, 75 or so would be really rather small centres, where the doctor concerned was probably doing more work related to leukaemia than haemophilia, and there was a relatively small number, as is still the case, of what's called "comprehensive" care centres.

So once a year there would be an annual general meeting of the whole organisation, usually a whole day business meeting, sometimes attached to a second day of science, with visiting speakers. But, in addition to that, every three months or so the comprehensive care

centre directors would meet up, usually in London, to discuss matters of more pressing business, and they were the ones that also set up all these various working parties: variant CJD, von Willebrand's, hepatitis, et cetera.

So they were a very active group, who met regularly and wrote protocols, and they would present everything to their colleagues at this annual general meeting, which, as you say, could be a very large meeting of 80/90 people maybe.

Q. In those days they were the reference centre directors, the other group, weren't they?

A. Yes, they were called reference centres.

Q. And it looks, just again in general terms, from having read a number different sets of minutes of the AGMs, as though from time to time the gathering would vote. So they might vote on what was the appropriate step to be taken in relation to something. Is that right?

A. Yes, there was a proper constitution and each director had voting rights.

Q. Right. I hope this doesn't sound too awful but I actually have four different documents relating to this meeting. A lot of people seem to have produced their own notes. Look firstly at the minutes, [SNB0017419]. This is only 1982, so you are not yet the

director in Kent but you were there; we can see your name. It's on page 2, I think, actually, if everyone just wants to see that. Yes, there you are. You are representing Dr Barkhan?

A. Dr Barkhan was my director at Guys, who wasn't very well, so I represented him.

Q. Do you actually remember this meeting?

A. Yes.

Q. Is that for a particular reason which is relevant to the Inquiry?

A. No, I think it was the first time I had been to such a meeting.

Q. Right. Now, really the only thing to look at in the minutes is page 10 at [SNB0017419]. I think we are into AOB by this point. At the bottom of the page we can see "The acquired immuno-deficiency syndrome":

"The Reference Centre directors had asked Dr Craske to look into the report from the United States of this syndrome, mainly in homosexuals but including three haemophiliacs. It appeared that there was a remote possibility that commercial blood products had been involved."

Without going back to it, I don't think Dr Evatt used the word "remote" in the MMWR but anyway:

"There was a remote possibility that commercial

blood products had been involved and Dr Craske asked the directors to let him know if they had any cases. The working party was considering the implications of the reports from the USA."

That would be the hepatitis working party in fact, I take it?

A. Yes.

Q. If we look at [DHF0016837], this is another redacted document but we can just see that someone has written along the top, "Received in confidence from the Haemophilia Society." By this time the Haemophilia Society had appointed Mr Watters as a coordinator. Do you remember Mr Watters?

A. Yes. By the way, the Haemophilia Society was always invited to attend the annual general meeting and they were always invited to make a short presentation about matters related to the society. David Watters was for a number of years the chief executive of the society.

Q. Thank you. Just to look at his note, he has summarised what he says are items of particular interest, rather than a comprehensive report of everything discussed at the meeting. He talks of the Reference Centre directors' reports, the annual returns, BPL Elstree, and then:

"The hepatitis working party ... "

I suspect that the name that has been taken out there is probably Dr Craske and we can see that from the other reports of the meeting:

" ... produced statistics on the incidence of hepatitis, which I found largely incomprehensible."

I am not quite sure what I should ask you about that, Dr Winter. It sounds really as though he has rather tuned out perhaps at the presentation of statistics on the likelihood of contracting hepatitis from commercial or NHS concentrates. But he does say:

"It appears from a study at Oxford that the risk of contracting hepatitis from large pool NHS concentrates is unexpectedly high."

A. I think the key word there is "NHS". I think that this is the point I was making, that, you know, the society at that stage were really very strong on promoting the use of NHS concentrate. They had concerns about the use of commercial concentrate, which many patients shared, and what is surprising him here is that this report is indicating that NHS concentrates might also transmit to a significant degree a form of hepatitis.

Q. Yes. So, put like that, Dr Winter, I think we can all understand why that would strike him as particularly worthy of note.

Look then at the next record, which is [SNB0017431].

This is not signed but without taking up too much time, I'm reasonably sure it is written by Dr Perry but we will put that beyond doubt when Dr Perry comes and we ask him.

This is his note of the meeting and if we look two pages in, at SNB0017433, he is taking notes on matters of relevance to PFC and he has noted down the statistics. If we look at the bottom of that page:

"The hepatitis working party ... "

He says:

"The following results of the study were presented."

Not a particularly large study, I guess, 32 patients, of whom 28 had adequate data, and then those who had a history of Factor VIII or IX transfusion, 26.

Then, if we go to the next page, the little table, it says that there were nine patients who had no record of receiving concentrate and of those who had had no previous concentrate, all nine seemed to have got NANB. And the little note beside that, a footnote effectively, is that seven out of the nine received NHS concentrate. So Dr Perry from the protein fractionation centre, I suppose he would be struck by that as well.

A. I don't really understand that data, I have to say. Perhaps you could ask him to clarify.

Q. We actually have quite a bit more data on that particular study, including the published article, which eventually appeared the following year.

Then go to the next page, 7435, heading "Liver disease in haemophiliacs", and perhaps particularly looking at the heading "Raised liver function tests", LFTs:

"Abnormal liver function tests were more than 50 per cent."

Perhaps that doesn't surprise you in the context of everything we have been saying.

A. No, it doesn't surprise me.

Q. And then he says:

"49 per cent of haemophiliacs on only cryo have evidence of CAH ... "

Would that be "chronic active hepatitis"?

A. Yes, it would be, yes.

Q. " ... or history of infection. Therefore cryo no better than concentrates? The main conclusion was there is not a lot to choose between commercial, NHS or cryo Factor VIII with respect to hepatitis."

That's perhaps slightly clearer than the table?

A. Well, the table wasn't very clear at all. These are very small numbers of patients, aren't they, really, and that's why the percentages are perhaps not really what

we would expect them to be.

Q. Then finally, at least on this meeting, could we look at [SNB0017494]? The writer of this note is Dr Frank Boulton because he has signed it. Dr Boulton is from the Blood Transfusion Service, Edinburgh and Southeast Scotland Blood Transfusion Service, and he also has a note about AIDS. He has got the statistics, the figures, that we have already looked at. I don't want to take up time with that. But could we look at SNB0017502. That will be page 9 of this, I guess. A similar sort of note underlined there:

"A first exposure to VIII or IX will cause non-A non-B hepatitis."

Then a heading at the bottom of that page, "Acquired immuno-deficiency syndrome":

"This is a wasting disease with deficient cell-mediated immunity, possibly associated with an infectious element ...

"Mortality 40 to 50 per cent.

"Three cases have occurred in haemophiliacs in the USA, possibly associated with parenteral drug abuse."

That's puzzling, isn't it, Dr Winter, because the reference to drug abuse, it is not only not in the MMWR report, the MMWR report actually says that they have no history of drug abuse. Do you have any theories as to

where that might come from?

A. Let's just reflect on where they were at that time. It is September 1982. Where they are coming from, both as doctors and with all the patient body, is, if you like, "We really have so much benefit from the use of these concentrates, we don't really want to hear about any problems with them unless we can find a very convincing reason so to do." I think there was a feeling at the time that, you know, these are very small numbers, the three patients, they are in America; can we be absolutely sure that they weren't part of some other risk group. I mean, it clearly says, as you say, that they weren't drug addicts, but I think the feeling at the time was we just don't have enough evidence at the moment, just based on three American patients who we maybe don't know enough about.

The other part of the pattern at that time was that always a lot of attention was paid to Germany. In Germany, particularly in the Bonn centre, they used spectacularly high quantities of Factor VIII. I think in fact the Bonn centre one year used more than every American centre put together, and one of the things that was said regularly at this time was, "If this is a new disease and it is in blood, why aren't the Germans getting it because, if anybody is going to get it, the

Germans will."

So I think this was another part at that particular time, September, of what you might call the stance of UKHCDO. All this would change within three or four months, as we will see in a minute, doubtless, but I can only think that at that time, with such a small number of cases -- no British cases, no German cases, three American ones -- it wasn't the basis for any further action beyond Dr Craske saying to everyone, "Please let me know if you see anything like this."

Q. Yes. I think perhaps, Dr Winter, just what's striking, when you look at it, admittedly in hindsight but look at it from a position of neutrality, is that firstly there is this reference to the possibility that the cases were associated with drug abuse -- and it is not really evident where that has come from -- and, secondly, that the possibility of transmission via commercial Factor VIII is being described as remote. We saw that in the official minutes as well.

I don't know if you would accept this: They do seem to be at least a bit of a gloss on the information that's available from America.

A. I think the sentiments might have been more cautiously phrased, mightn't they? They might have used sentiments like, "There seems to be no evidence at this time," but

the UKHCDO would instigate studies to look further at the problem, et cetera. I mean, these minutes were usually written by a doctor in a hurry, coming back from the meeting and, you know, "I must get minutes out," and they didn't necessary reflect -- how could they? -- what actually might be eight hours of meeting.

THE CHAIRMAN: Ms Dunlop, if you are turning to a new topic, I have got a problem.

MS DUNLOP: Yes, I know. Well, can I just finish 1982? I have got one more document.

THE CHAIRMAN: Yes, okay.

MS DUNLOP: Just so that we can make a start a little bit further on tomorrow morning. I just wanted to highlight lastly [LIT0010540], which is another MMWR. It is 24 September 1982. I won't ask you any questions about it, Dr Winter, but I'll just point out that the incidence of AIDS has roughly doubled every half year since the second half of 1979. Then the mention of people with haemophilia, which is at the foot of the first page. Then the editorial note on the next page suggesting that the eventual case mortality may be far greater than the 41 per cent rate noted and that perhaps haemophilia A is an identified risk factor.

So that was really all, sir. This one, for some reason, isn't in the Preliminary Report.

THE CHAIRMAN: No.

MS DUNLOP: So just to get it into the notes. Then that enables us to start in January 1983 tomorrow.

THE CHAIRMAN: Thank you very much.

(3.57 pm)

(The Inquiry adjourned until 9.30 am the following day)

I N D E X