Wednesday, 23 September 2020

(10.00 am)

SIR BRIAN LANGSTAFF: Ms Richards, you are going to deal with knowledge of the risk.

MS RICHARDS: Yes, sir.

SIR BRIAN LANGSTAFF: Today, just so that everyone knows where we will be in terms of timing, because we aren't subject to the witnesses giving his evidence, Ms Richards will have her timing under control, I understand.

MS RICHARDS: I hope.

SIR BRIAN LANGSTAFF: So what we will aim to do is we will aim to finish no later than 4.30. There will be, again, 45-minute breaks in both the morning and in the afternoon. The afternoon probably little bit earlier than it was yesterday to divide up the afternoon rather better. 45 minutes to enable you to have the time to go safely, at distance, to pre-allocated seats for refreshment.

So that's what we will do so you know where you are and what the timing will be.

Ms Richards.

Presentation by MS RICHARDS

MS RICHARDS: So, sir, if I can just start by explaining the purpose of today. Today is the provision of

a chronological and historical overview of material relevant to the knowledge of risk of infection from blood and blood products. It will be undertaken by showing contemporaneous materials and those will be drawn from a range of different sources, Government, scientific journals, correspondence, meetings and so on as well as media, and we'll be showing a number of documentaries or documentary excerpts in the course of the day.

The purpose of the presentation is twofold: it's to place relevant material into the public domain. So core participants have already been provided with copies of all the material that will be referred to and with a detailed chronology relevant to this issue, but the purpose of today is to ensure that the material or some key parts of it is shared with those who have not had the opportunity to work through what will be thousands of pages of material, and to ensure that the wider public is enabled to understand what was or was not known at various relevant times.

The second purpose of today is to provide a backdrop to the evidence that's going to be heard from witnesses over the coming weeks and months, from clinicians in the first instance and, in due course, from politicians, civil servants and others.

I should say what today is not: it's not going to be examining in any kind of detail what was known by a particular individual or a particular organisation, or what should have been known by that individual or organisation, nor is it going to be looking in any kind of detail at what was done in response to those risks. Again, that will be material that's explored over the coming weeks and months with witnesses.

We're very grateful to core participants who have suggested additions to the material that's in the chronology. Some of that's been incorporated in today's presentation but we would welcome any continuing suggestions and the chronology can be updated with any additional material that core participants or indeed others think is relevant and can bring to our attention.

So, sir, broadly speaking the presentation falls into four categories chronologically. The first will be looking at the developing knowledge of risk of the transmission, through blood or blood products, of hepatitis from the 1940s through to the 1970s.

The second is to look more particularly at the developing knowledge about non-A non-B hepatitis in the course of the 1970s and knowledge of the

seriousness of the condition.

The third is then to look at the developing picture in relation to HIV and AIDS in the first half of the 1980s.

The fourth then picks up the picture going up into 1991 in relation to developments, the discovery of hepatitis C and some key dates and documents in relation to that.

I don't propose, for the purposes of this presentation, to look beyond 1991, although clearly the years after 1991 contain much significant material, but those will be explored in later stages of the Inquiry's hearings and vCJD specifically will be the subject of a discrete hearing in due course next year. So I won't be touching on vCJD today.

The other point in relation to timing is I'm not quite sure how long today is going to take. If I don't get through the material that seems most important we'll continue tomorrow rather than sit late before moving on tomorrow to look at the actions of Professor Bloom and the Cardiff Haemophilia Centre.

Sir, there's no single right place to start but I'm going to start in the 1940s with observations of jaundice in army personnel and its relationship to the vaccination against yellow fever.

Henry, could we have, please, RLIT0000209.

This is a document entitled "Jaundice in army personnel in the western region of the United States and its relation to the vaccination against yellow fever". It's the second of two papers published in the American Journal of Hygiene in 1944. The events to which the paper relates focus on the high prevalence of jaundice in troops in the spring and summer of 1942 in circumstances in which the troops had been vaccinated against yellow fever.

It is a very long article, I am just going to go to a small number of points from it, but I am very grateful to core participants who have suggested some shorter precises of this issue. I am going to give a couple of references that don't need to come up on the screen; it's for the benefit of others who may want to read about this issue.

There are more recent analyses of this issue at RLIT0001238, RLIT0001234, and RLIT0001237. Those are all later documents that look back but I'm focusing, as I said, today on contemporaneous material.

Henry, could we go, please, to what I think should be page 39 of the document. I'm sorry, my apologies, I am using the internal pagination. So it will probably be page 5 on the documentation you have,

thank you.

So we can just pick up here a report in 1937, in England.

If we look halfway down the page, Henry, if we see the whole part. Thank you.

"England Post Vaccination Jaundice. In 1937, Findlay and MacCallum reported that in the course of 4 and a half years they vaccinated approximately 2,200 persons against yellow fever and had observed 48 cases of jaundice occurring from 2 to 7 months after vaccination."

Then if we look at the right-hand column, Henry, could you highlight the first 10 or 12 lines of the second paragraph, beginning "Findlay and MacCallum". Is it possible to highlight that in yellow so it's easier for others to read.

Anyway, those who are looking will be able to see what passage I'm referring to. So it refers to:

"Findlay and MacCallum were firmly convinced that the jaundice was not caused by the yellow fever virus itself. In a later report, in 1939, they analysed in detail the various factors involved in this episode and came on the conclusion that the causal agent of the jaundice was a virus that had been cultivated serially in tissue cultures in symbiosis

with the yellow fever virus and that it must have been introduced into tissue cultures in association with human serum ..."

So that's the key issue here: human serum:

"... presumably derived from a donor who was either in the incubation period or actually suffering from a mild subclinical attack of epidemic catarrhal jaundice."

Then if we could go, please, Henry, to -- I will try to give you the right references -- page 58 of the article, which I think might be page 24 of 73. Yes, that's it.

If we look down the bottom half of the page, please, so we can then, picking up on what had been observed in 1942:

"Jaundice in the military forces in the United States and elsewhere following vaccination against yellow fever.

"As stated in part 1 of this report, information was received in March, 1942, that in United States army personnel there was a considerable amount of jaundice which appeared to be associated with certain lots of yellow fever vaccine used for immunisation."

Then, Henry, if you could skip on, please, because there's a very detailed account of the

investigation, which I won't go to, to pages 54 to 55 of 73 -- it's page 89 of the internal pagination. Next page.

So if we pick it up under the heading "Conclusion", towards the bottom of that page:

"It has not yet been possible to demonstrate conclusively which of the various materials used in the preparation of yellow fever vaccine actually contained the agent responsible for the outbreak of post-vaccination jaundice. However, in view of other investigations that outbreaks of hepatitis have followed the injection of human serum alone, and also that it has been possible to transmit a very similar disease by direct blood or serum transfer from patients suffering from infective hepatitis to healthy volunteers, human serum falls under suspicion much more definitely than any other substance in the vaccine."

It's instructive to note, if we go to page 103 if you are using the internal pagination, Henry, or it's pages 68 to 69, thank you, we see -- if we go down to the bottom of the page, please, Henry -- "Recommendation", we see that in the course of this investigation the investigative team in April 1942 made recommendations to the surgeon general of the

army to suspend the use of vaccinations in which human serum had been implemented and to use, effectively, different vaccinations and that had the desired effect of stopping the particular attacks of jaundice that had been observed.

Could we then turn from America to, still within 1942, in the war years, this country and go to DHSC0100008_024, please.

We can see this is headed "Emergency Blood Transfusion Services delayed jaundice". It's an internal DHSS document and it's a note of a discussion held in Dr Taylor's room on December 1st, 1942, with a number of doctors in attendance:

"Dr Taylor said that recent investigations suggested that blood transfusion might result in delayed jaundice and the meeting had been called to decide whether and how hospitals, maternity units and general practitioners should be informed of the latest developments on the subject and whether any preventative administrative measures were possible."

Then Dr Bradley gave an account of the history of the appearance of jaundice believed to be due to the introduction of human serum.

We can see from this that going back to the 19th century there had been issues of concern as to the

connection between human serum and jaundice, so we have 1885 in Bremen 191 cases of jaundice follow the use of humanised lymph. At (2) measles convalescent serum, a batch of serum used on 109 children resulted in 41 cases of jaundice and eight deaths. On another occasion 57 c.c. injected and 14 children gave six cases of jaundice and one death. That was picked up by -- considered by the Chief Medical Officer of the time in the late 1930s.

We then have the reference to yellow fever vaccine, reports of jaundice in Brazil, in the American forces -- that's the material we've just been looking at -- reference to convalescent mumps plasma with 87 cases of jaundice. All the above vaccines et cetera contained human serum.

Then we have reference to blood transfusion. The first case of jaundice following a transfusion was notified from Wolverhampton; subsequently eight cases of jaundice resulted from 35 transfusions of serum given for peripheral vascular disease.

Then it says this --

NEW SPEAKER: 36 I think.

MS RICHARDS: I'm sorry, 36, yes apologies:

"In all 13 cases of jaundice apparently resulting from transfusion were known so far to have

occurred in England, but it had not been possible to plan any follow up of transfused patients. Not possible to rule out the possibility of natural causes but certain information suggested there might be a distinguishing clinical picture in the case of jaundice caused by the introduction of human serum."

Then if we have over the page we can see reference to certain measures having already been taken, discussions with the Medical Research Council, Dr Panton and Dr Proger and the Blood Transfusion Officers:

"We are told that the MRC Transfusion Committee had convened a small *ad hoc* subcommittee to enquire into transfusion jaundice."

I emphasise this is in 1942.

"With the exception of the CMO's reports in '37 and '38 on the measles case, none of the known cases had been published but Dr Bradley has now been asked by the CMO [Chief Medical Officer] to publish in The Lancet a memorandum which he had prepared on the subject with a view to bringing it to the notice of blood transfusion officers and general practitioners and urging them to record the batch numbers of transfusion materials used and any cases of jaundice resulting."

Then if we just go down to the bottom of the page:

"It was agreed that the following action should be taken: (a) Dr Bradley agreed to word his memorandum for The Lancet in such a way as to prevent unnecessary alarm. He would stress the importance of recording the batch number of materials used in transfusion and of reporting cases of jaundice following blood transfusion."

There's a reference to general practitioners being asked to report matters to the hospital, and then:

"(b) After the publication of this article the Ministry would issue a DGL drawing attention to it and asking hospitals and maternity units to maintain case records, do all that was possible to follow up patients who had been transfused and report any cases of jaundice to the supply depot. The DGL would also stress the importance of making a senior officer in each hospital responsible for transfusions."

So it can be seen that at a senior level this was regarded as a significant and important issue in 1942.

The memorandum that's referred to there that's going to be published in The Lancet we have at

NHBT0000091_011, please, Henry. We can see the date of its publication is January 16, 1943. It's published in The Lancet. The title is "Homologous serum jaundice". It's a memorandum prepared by medical officers of the Ministry of Health.

I won't go through the detail of it but if we could turn, please, to -- it should be the fourth page, Henry -- that's the one. We can see a heading towards the bottom on the left-hand column, "Transfusion hepatitis". Reference is made to various incidents and then if we can pick it up on the right-hand column, Henry, the paragraph beginning, "The appearance of this phenomenon ..." I don't know whether it's possible to highlight that. It's about the fifth paragraph down, please:

"The appearance of this phenomenon [that's the hepatitis jaundice appearing after some form of receipt of human serum] was anticipated at the Ministry of Health where information had previously been received of another grave case of jaundice following whole blood and plasma transfusion ... on August 13, 1942, a meeting of the principal blood transfusion officers was called to inquire, *inter alia*, whether this was an isolated case or whether transfusion was more frequently followed by hepatitis.

It transpired that not until August 12 did the cases in the EMS hospital [that is the particular cases that are being looked at in part of the memorandum] come to the notice of the transfusion officers. Since then the condition has been observed at three other hospitals. The total of known cases following transfusion is now 12. It must, however, be remembered that no systematic follow up of transfused patients has been attempted and that since an association between transfusion and late jaundice is unlikely to be recognised spontaneously, it is not to be expected that such remote sequelae would be brought to the notice of the blood transfusion officers."

Then this sentence:

"For this reason it cannot be assumed that whole blood is innocent or that plasma is likely to be less icterogenic than serum."

If we go two pages further on to the last page, please, Henry, under the heading "Comment", this Ministry of Health memorandum concludes as follows:

"The examples of homologous serum jaundice collected in this paper make it clear that the subject is one of major importance. Our understanding of the mechanism has not advanced since 1937 when measles serum jaundice was first described. One conclusion is

now however, evident: any doubt as to the reality of the association is removed by the frequency with which hepatitis has followed the injection of human blood products. The probability that further cases will occur, particularly after transfusion, must be faced."

So that's The Lancet, Ministry of Health publication, 1943.

Can we then please have up on screen, Henry, DHSC0100008_051, please. It's not the easiest document to read. I have a handy translation. It's entitled, "Prevention of homologous serum jaundice memorandum to MRC Jaundice Committee on administrative and field aspects". It's authored by Dr Bradley. The date is 20 June 1944. There are just a couple of passages to read from this.

In the foreword, so this is the first paragraph:

"The observation that hepatitis may result from injection of homologous serum after a long interval has now been confirmed beyond doubt. At the present time, transfusion with pooled dried serum appears to be the source of greatest anxiety, although comparatively small quantities of this product have been used. With the greater use of transfusion in the treatment of battle casualties [pause to observe, obviously this is still during the Second World War]

a corresponding increase in jaundice may be expected. The problem of serum jaundice is not only an immediate one but may become of increasing importance as the use of dried human serum in therapeutics is developed."

Then if we go down to paragraph (d) at the bottom of the first page there's a discussion of the relationship between homologous serum jaundice and epidemic hepatitis and a reference to the yellow fever vaccine jaundice investigations. Then it says this:

"By comparison with the estimated mortality of epidemic hepatitis fatalities from homologous serum jaundice have been disproportionately numerous."

Then if we go over the page, please, to paragraph(f) on page 2:

"There is a strong suspicion that the severity of hepatitis varies with different batches of serum. Some kill and others produce relatively mild disease. It is also probable that serum hepatitis occurs without jaundice and that some patients may remain ambulant and uncomplaining."

Then we see under the heading administrative control, and again I emphasise this is in the 1940s:

"Although medical measures for the control of serum jaundice must wait on further knowledge concerning the nature of the jaundice producing agent

and how to remove it, much can be done in the way of prevention, without this knowledge by (a) avoiding unnecessary transfusion. At the present time serum transfusion should be reserved for life-saving procedures only; (b) restricting the size of pools", then a number of other matters about records, sampling and so on.

Then top of the next page, this is still within the list of suggested administrative preventative measures:

"As far as possible transfusing any individual patient with serum from one pool only."

Then (g):

"Taking greater care to exclude blood from persons suffering from hepatitis on the assumption that serum jaundice is simply transmission by unusual routes of the agent of epidemic hepatitis."

If we go to the penultimate page, please, next page, next page, next page, last but one page, please, that's it, could we have the second paragraph highlighted, please:

"It is our duty to follow up and study serum jaundice just as we should follow-up any other communicable condition. Knowledge will come quickly only if the collection and collation of information is

deliberate and purposeful. We should evolve a carefully proposed plan, and provide adequate facilities for it to be carried out."

Then we see there Ministry of Justice *(sic)* 20 June 1944.

SIR BRIAN LANGSTAFF: I think it is Minister of Health.

MS RICHARDS: Yes, Ministry of Health.

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: Then, please, Henry, if we could have --

SIR BRIAN LANGSTAFF: Just pausing there for a moment so that most people will know I think that homologous means from human beings as opposed to from somewhere else.

MS RICHARDS: Yes. Yes, it's essentially the association between human serum and hepatitis that is the focus of all of these documents in the 1940s.

We then have, please, Henry, DHSC0100008_095. This is a letter dated 21 March 1945 -- April has been crossed out and March added. It's from -- could we have the whole document, sorry, Henry. It is from the Chief Medical Officer W Wilson Jameson and it says this:

"Dear Panton, homologous serum jaundice, I have received reports, attached, that hepatitis with a high fatality is frequently following transfusion. I am

concerned for the future because blood products will continue to be used in civilian practice after the war and it would appear that the present experience amongst battle casualties provides an opportunity, which is unlikely to recur, for obtaining further information."

The documents to which he refers, the reports, I won't bring up, but they are all in the chronologies and the material that is disclosed to core participants.

Then we see -- if we have, please, Henry -- DHSC0100008_105, we can see that there is then what would appear to be, from the participants, a fairly high level conference held at the Ministry of Health on 26 March 1945. The title of the meeting or the notice: "Jaundice Following Transfusion". We can see present the Chief Medical Officer, a number of senior officials within the armed services, representatives of the Blood Transfusion Services, including Dr Panton, to whom the previous letter was addressed, and representatives of the Ministry of Health, including Dr Bradley, who had been the author of one of the documents that we looked at earlier.

We can see here, on the first page:

"Sir William Jameson told the meeting that the

Ministry of Health proposed to attempt to carry over into peace-time something of the transfusion arrangements that had been in operation during the war. Unfortunately, it was beginning to appear that a large number of transfused persons subsequently developed jaundice and some died. He quoted Dr Stocks' figures culled from pensions records and death certificates. Although this serious complication might pass without comment in war-time, it would seriously handicap peace-time administration. Information concerning this puzzling condition was at present being collected independently by several persons and he was anxious to establish an orderly system of accumulating and using the information."

Then if we could go to the third page, please, Henry, we can see halfway down the page, if we just go down a bit further:

"The Chief Medical Officer, summing up, said that, although the accounts given were somewhat contradictory [and the accounts had been from various different military and other personnel attending the meeting], there was some reason for believing that hepatic jaundice may follow blood transfusion and that some transfused persons died of hepatic necrosis but the position was not clear. Nothing definite had so

far been learnt from laboratory work and he hoped that epidemiological study might add something useful. This required a good system of recording and a free intercharge [that should be interchange] of information."

Then if we go to the fourth and final page please, Henry, just under the heading "Propaganda":

"It was agreed that nothing which might cause public alarm or discourage transfusion in necessitous cases should be done. The Chief Medical Officer suggested that sometimes transfusions were performed unnecessarily and that it might be wise to send some publication to institutions. Dr Drury suggested, and it was agreed, that the opinions of regional transfusion officers on this matter should first be sought at a meeting to be held on 5 April 1945."

Then, again still in the 1940s, if we could go to DHSC0100008_254, please, Henry, not going to go to the detail of these articles but just to note in terms of broadcasting to the wider medical profession what thus far has been to some extent conversations held internally within the Department of Health and with the armed forces, what we have here are three articles: Homologous Serum Jaundice; Homologous Serum Hepatitis; Two Cases of Homologous Serum Jaundice. We

can see they're printed from the proceedings of the Royal Society of Medicine in August 1946.

Again, without going into the detail, if we can have up on the screen, Henry, RLIT0000052, we now have a publication in the British Medical Journal. This is September 1946. It's an article headed "The incidence, incubation period, and symptomatology of homologous serum jaundice", by Spurling, Shone and Vaughan and we can see here in the introduction it says:

"Jaundice has been recognised with increasing frequency as a sequela of transfusion with whole blood, plasma or serum."

Reference is made, amongst other things, to the Ministry of Health memorandum that we have looked at.

"It's generally agreed that such jaundice is indistinguishable from, and of the same aetiology, as the jaundice following the use of convalescent serum, vaccines containing human serum and syringes contaminated with human blood. This jaundice is commonly called homologous serum jaundice.

"Since certain of the cases reported after transfusion have proved fatal, it appeared important to determine if possible the incidence of this complication since it might well be that the risk of

hepatic necrosis was greater than the risk incurred by withholding transfusion. Records of blood products issued from the northwest London area since 1940 being available, a follow-up of patients who had received transfusions in this area was, therefore, instituted in 1944 with a view to determining the incidence of homologous serum jaundice following transfusion, its incubation period and the symptomatology."

The article then sets out the figures from that particular follow-up. We'll see, if we look at the third page, it's in relation to the findings of this report.

Go -- right-hand column, Henry, just the paragraph above the heading "Summary", please.

What this study found was that:

"The character of the jaundice in the 77 cases here recorded was, with one exception, mild."

It says:

"This is in accord with the majority of other observers, but it must not be forgotten that a definite mortality after both transfusion jaundice and syringe jaundice has been noted."

Also relevant to note, from the 1940s still, in 1947, was the identification of higher risks associated with pooling of blood donations and we'll

go to just one document in that regard.

Henry, it's RLIT0000054, please.

We can see this is an American article, Homologous serum jaundice in recipients of pooled plasma". It's published in October 1947 by Brightman and Korns and I will just pick it up with the first paragraph:

"The ready availability of pooled plasma, whether secured through commercial channels, state departments of health or local blood bank programs, has been a boon to medical practice. However, the fact that plasma may carry a virus capable of inducing hepatitis in the recipient has created a new public health problem of major importance."

If we then go on, please, Henry, to the fourth page of this document, left-hand column under the heading "Comment" -- just scroll down -- so, "Comment":

"A follow-up investigation of a large series of persons who received transfusions with pooled plasma has indicated that this form of therapy carries a significant risk of a serious and possibly fatal complication."

Then figures in relation to upstate New York are provided.

Then if we go to the next page, please, Henry, under the heading "Summary", I will just read this:

"1. Follow-up of 649 patients who received transfusions with dried pooled plasma revealed a subsequent incidence of homologous serum jaundice in 4.5 per cent.

"2 the causative agent appears to be widely distributed but the attack rate is variable.

"3. The attack rate was significantly higher among persons who were 50 years of age or more. No relation of the attack rate to the amount of plasma administered could be demonstrated.

"4. Investigation of 51 deaths attributed to acute hepatitis revealed 15 cases in which the patients had received transfusion therapy during the six months prior to death. 12 of these had received plasma only.

"5. 12 deaths attributable to homologous serum jaundice were reported in upstate New York during a seven-month period."

Then this at 6:

"Plasma as well as other forms of transfusion therapy, should be administered only when the clinical indications are absolute, so that the benefits to be derived clearly outweigh the risk of contracting

homologous serum jaundice."

Now, turning back from America to the United Kingdom, and we've now reached the 1950s.

Henry, could we have DHSC0100010_405.

This is a letter dated 6 January 1950. It's from Dr Drummond of the Regional Transfusion Centre in Cardiff and it's to Dr Maycock at the Ministry of Health. It says this:

"I have decided to abandon large pool plasma filtration. I do not feel I can justifiably continue to issue large pool plasma which has an incidence of homologous serum jaundice of 10 per cent, as opposed to 1 per cent for small pool plasma. Were a case of homologous serum jaundice to go to the law courts, and large pool plasma to be implicated, I don't think the court would be kindly disposed. It might argue we ought not to have issued large pool plasma since the incidence of homologous serum jaundice is ten times as great as after small pool plasma. It might be argued that the issue of large pool plasma is unjustifiable since it is practicable to make small pool plasma, either filtered or unfiltered. Such an argument would be unanswerable."

Could we then, please, have, Henry, and I'm hoping I've got the right reference here, RLIT0000215.

Yes, so we can see a World Health Organisation publication. This is in March 1953. The committee, the expert committee on hepatitis set up by the World Health Organisation had met in July 1952 and I'm not proposing to go to any particular part of this document but you'll see that by this time hepatitis, including serum hepatitis, is as it were on the agenda of the World Health Organisation on an international stage.

Then if we could --

SIR BRIAN LANGSTAFF: I think that was the document or at least part of the documentation which I referred to yesterday when I was asking questions of Dr David Owen.

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: For those who are interested, the passage I was or the principles I derived from it are set out at part 10:

"Prevention of the spread of hepatitis viruses A and B by human blood and by its products."

MS RICHARDS: Yes. It's an important document and one that we will no doubt return to with some witnesses in due course.

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: We've been in Wales with the Regional

Transfusion Centre. The next document takes us to Scotland, PRSE0000157, please. This is a memorandum from the Scottish Home and Health Department which I have a feeling I might have referred to yesterday as the Scottish Health and Home Department.

16 December 1964 Scottish hospital memorandum number 89, 1964, "Scottish National Blood Transfusion Association, hospital blood transfusion arrangements and the supply of blood products in clinical use".

Then we'll see it's a memorandum describing the work of the Scottish Blood Transfusion Service and containing some suggestions as to the management of hospital blood banks, reminds medical officers of the risk of transfusion therapy and gives guidance on how the risks may be reduced. That's in paragraph 1.

Then if we could go please to the first page, Henry, paragraph 11 the memorandum says this:

"All blood for transfusion must be regarded as potentially contaminated, and care must be exercised to ensure correct conditions of storage. This applies not only during storage in the blood blank, but also during transportation."

Then skipping over a sentence this:

"The most important transmissible disease in this country is homologous serum jaundice or serum

hepatitis, the incidence of which is 5 per 1,000 recipients of blood or small pool plasma. No transfusion should be undertaken unless the benefits outweigh the risk of hepatitis."

Then it says this in 12:

"The avoidance of transfusion accidents is primarily the responsibility of those medical officers in charge of the patient ..."

Pausing there, whether that is intended to encompass the risk of hepatitis referred to in the previous paragraph is unclear:

"... and of those in charge of the blood bank and laboratory. The ramifications of the organisation of a blood transfusion service within a hospital are so widespread that it should be looked at from time to time by the medical staff committee ..."

We are now in the 1960s and there are a number of reported materials in the course of the 1960s onwards showing the emergence of knowledge of the Australia antigen. I am not going to go to the majority of those documents but it's an important part of the chronological development of the knowledge of hepatitis B and for those who are interested, you don't need to put this up on screen, Henry, but there is an article in February 1965 which describes the

emerging knowledge of the Australia surface antigen at PRSE0001518.

What I want to pick up however is a publication in August 1965, PRSE0003897. Again, we're drawing on a range of materials to show how knowledge may have been -- how risks may have been understood by different cohorts of practitioners. This is a publication called "The Practitioner" and it's, this particular part, complications of blood transfusion, is authored by Jean Grant, the then director of the Regional Transfusion Centre in Oxford. If we could go please to page 6 of this, Henry, under the heading "Transmission of disease", we can see there what is set out under the heading "Homologous serum hepatitis":

"The development of homologous serum hepatitis is a hazard which besets rather less than 1 per cent of recipients of whole blood or small pool plasma."

There is reference there to the MRC publication in 1954:

"It is caused by the transmission of a virus from a carrier donor to a susceptible patient. The donor is probably not aware that he is a carrier. He gives no history of ever having had infective hepatitis himself ... and no single test or battery of

liver function tests has yet been devised which would reliably distinguish carriers of the virus from normal subjects."

It then goes on to describe how recipients vary in their susceptibility. Then the next paragraph:

"Some patients suffer no upset from the transmitted virus. Some may have only a transient liver dysfunction, with or without jaundice, and yet others may develop a rapidly fatal hepatic necrosis."

Then reference is made to attempts thus far not particularly satisfactory of finding a means of killing the virus in the blood.

If we go to the last page, please, of this document I think we can see from the way in which this last conclusion is expressed that this is intended to be advice from the Regional Transfusion Centre to practitioners in the field. Under the heading "Conclusion":

"The practitioner should satisfy himself that it is really necessary to give blood and that no other treatment would be equally efficacious, even though it might take a little longer to achieve results. He might even benefit his patients by occasionally having the strength of mind to make the unfashionable decision not to transfuse. The hitherto healthy

patient can well afford a one pint haemorrhage without replacement, after all as pointed out by Chassar Moir the blood donor himself lost a pint without anybody feeling that he ought, therefore, to receive a transfusion."

Then, Henry, could we please have RLIT0000217. This is one of a number of documents authored by J Garrott Allen in the United States. This particular publication is I think 1 April 1966. It's headed, "Post transfusion hepatitis, a serious clinical problem", and it suffices I think only to look at the summary on this page in italics:

"The risk of serum hepatitis from transfusions derived from prison and skid row populations is at least ten times that from the use of volunteer donors."

This is being said in April 1966:

"For every 100 patients receiving a single transfusion the attack rate is 0.3 per cent where the donor is of the family or volunteer type and 3.2 per cent when the donor is from a prison or skid row population. The most practical method of reducing the hazard of serum hepatitis from blood are to limit the use of blood by giving one transfusion instead of 2, 2 instead of 3, et cetera, and especially by

excluding, if possible, all prison and skid row donors. It is urged that the state and federal control of the quality of blood used for blood transfusions be studied with the possibility that measures may be taken to increase its safety. If it is necessary that blood from prison and skid row donors be used to meet the demands such blood should be labelled as carrying a significantly increased hazard of transmitting serum hepatitis in order that the physician prescribing blood may take the necessary precautions."

Then from the US back to the UK with RLIT0001219. This is the same year, August 1966, and the relevance of this is just to show that the same issue is raised in a leader in the British Medical Journal in that year under the heading, "Transmission of disease by blood transfusion", where it says this:

"Hepatitis, syphilis, malaria and brucellosis have all been transmitted to patients who were given whole blood or blood products. Hepatitis is by far the most serious disorder transmitted in this way ..."

Then there is a reference to the different incidence rates depending upon the size of the pool. Then it says this:

"This important hazard of blood transfusion is

not as widely appreciated as it should be."

Then reference is made to one reason for that possibly being the comparatively long incubation period.

If we could then please have up on screen, please, Henry PRSC0000821.

This is a letter dated -- or a publication again in the British Medical Journal 5 November 1966 and it's a letter from Professor Zuckerman from the London School of Hygiene and Tropical Medicine. The left-hand column please, Henry, the article headed, "Blood transfusion and infectious hepatitis". Professor Zuckerman who was based then at the London School of Hygiene and Tropical Medicine was a leader in the field or hepatitis at this time, as we will see from later materials. He said this:

"There are at present no specific tests for virus hepatitis but the serum transaminase levels have proved a sensitive index of liver damage. These tests have not been carried out in the small series of patients reported by [he refers back to an earlier publication] and it should be difficult to draw any valid conclusions from their results on the absence of anicteric post-transfusion hepatitis in 82 patient who received 222 pints of blood. Hazardous and misleading

to attempt to translate these results into national figures. Estimates of the risk of hepatitis in blood recipients in the USA vary from 0.3 to 4.13 per cent and from a number of reports it was estimated that the overall mortality from post transfusion hepatitis could be as high as 27.5 per cent. Even more significant is the fact that although infectious hepatitis cannot be considered a major cause of death it nevertheless ranked in 1959 in the USA second only to influenza among the deaths attributed to acute virus infections."

Then if we could go to the top of the next column, please, Henry:

"In this country an estimate of the size of the problem of hepatitis cannot be made since hepatitis is not notifiable on a national basis. Nevertheless it should be a matter for considerable anxiety that there are indications that the number of deaths from hepatitis after cardiac surgery in some centres exceeds the mortality from surgery. Therefore, before we can aspire to undertake any preventative measures the first step should be the notification of hepatitis and the establishment of a follow-up system for all patients who have received blood transfusion. The problem is surely of such importance as to preclude

any attempts to guess the actual figures for hepatitis."

So that is Professor Zuckerman in the mid-1960s recommending the establishment of a follow-up system for all patients receiving blood transfusion.

There's a further document from Professor Zuckerman, Henry, at RLIT0000220. You don't have that? Don't worry. We can come back to that if need be.

Can we then go to PRSE0003714. This is, September 1969, an article in the British Medical Journal or a letter in the British Medical Journal from the Royal infirmary in Liverpool, headed "Serum hepatitis in a haemophiliac". It says this:

"Serum hepatitis after the use of cryoprecipitated antihaemophilic globulin is unusual."

Refers to a reported case, and then says:

"We report a second case with a fatal outcome."

The letter then details the particular case, which I won't take time going through, but if we go to the concluding two paragraphs of the letter it says this -- Henry, sorry, you can go back up. That's great.

"The clinical and necroscopy findings here are fully compatible with a diagnosis of serum hepatitis.

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."

I'm not going to go to it but there is then in the British Medical Journal two months later, in November 1969, another case of serum hepatitis in a haemophiliac patient reported in Belfast, and the reference for those who are interested is PRSE0004488.

Sir, that brings me to the 1970s, and the next document is one that might take a little longer to look at, so is that a convenient moment to break?

SIR BRIAN LANGSTAFF: Yes, it is.

So we will take our break now for the next 45 minutes and be back at 20 to 12.

(10.56 am)

(A short break)

(11.41 am)

MS RICHARDS: Sir, we've reached the 1970s.

In July 1970 the Department of Health convened

a meeting to discuss the problems of Australia antigen in relation to blood transfusions and associated matters.

In September of 1970, following that Department of Health meeting, the Advisory Group on Testing for the Presence of Australia (hepatitis-associated) antigen and its antibody -- it's a rather lengthy name of a group -- was formed under the chairmanship of Dr Maycock. We have its first report at PRSE0000190. It's, again, quite a long document and so I won't go through all of it.

We can see if we go to the second page, please, Paul, paragraph 2 we have the terms of reference, to advise the health department -- sorry, I should pick it up, in fact, before that because we can see its geographical scope:

"... we were appointed in September 1970 as an advisory group jointly by the Department of Health and Social Security, the Scottish Home and Health Department and the Welsh Office, with the following terms of reference:

"To advise the Health Departments on:

"i. the organisation of and responsibility for testing blood donations and other specimens of blood for Australia (hepatitis-associated) antigen and its

antibody in the hospital service;

"ii. the provision of reagents, choice of methods and whether, and if so, what kind of, training facilities are required;

"iii. the scale of accommodation, staffing, equipment and other services necessary to implement the group's proposals."

We can see that their members included consultant virologists, directors of Regional Transfusion Centres and a senior technical officer of the Public Health Laboratory Service. They met first on 5 October 1970, met on five subsequent occasions, and then produced this particular report.

If we go, please, to page 4, paragraph 6, Paul, we can see it's there said:

"Knowledge of all aspects of Australia (hepatitis-associated) antigen is accumulating very rapidly. Our recommendation should therefore be regard as interim ones and they may have to be modified in the light of new information."

So this was, as it says there, part of the developing knowledge of what would soon be identified and labelled as hepatitis B.

If we then go to the next paragraph, please, next page, paragraph 7, we can see there:

"Australia (hepatitis-associated) antigen is the name used in WHO memorandum 1970 for the antigen apparently associated with the infective agents thought to be the cause of serum hepatitis."

Then various other names given for it are there set out.

"The association between the antigen and serum hepatitis commonly accepted as the most frequent form of hepatitis observed following the injection of blood and blood products is well-established and the antigen can now be detected by a variety of laboratory tests."

Then if we go to the next paragraph, please, paragraph 8, it says:

"Although the hepatitis agent maybe less widely dispersed in the UK than in some other countries, the institution of testing blood donations for Australia antigen should reduce the incidence of serum hepatitis, which is the most serious complication of transfusion and so avoid suffering and disablement and even death."

So the aspiration from the early '70s was that the testing that was beginning to be available would enable there to be a reduction in the incidence of serum hepatitis. We will see as we go through the 1970s how that panned out.

If we go then please, Paul, to page 22. It's headed chapter 10, "Summary of principal recommendations". Thank you. So, "Summary of principal recommendations":

"For the reasons already given we make the following recommendations: (1) the Regional Transfusion Centres should begin at the earliest possible date, to test all blood donations for the presence of Australia-hepatitis-associated antigen and its antibody."

Then reference is made in the next paragraph to the form of testing and recommendations in relation to staffing, safety precautions, accommodation and equipment. Then if we go to (iv):

"A donor found to be antigen or antibody positive should not be allowed to continue as a donor of blood intended for clinical use and he should be told so and invited to give permission for his GP to be informed."

Those were the recommendations at the beginning of the 1970s. We then will move on to RLIT0000076, please, Paul. This is April 1971.

It's a letter again from J Garrott Allen, the professor of surgery at Stanford University School of Medicine to a medical publication, California

Medicine, in April of '71, "Post transfusion hepatitis", and he says this:

"First, the numbers of patients who develop post transfusion hepatitis will be about 1 in 33 transfused when the blood from a volunteer population is contaminated with as much as 44 per cent of blood from prison donors. The numbers of patients with transfusion hepatitis, under these circumstances, who will be able to show disability or who will die of this disease, will be approximately 0.9 per cent of the total transfused. If one considers only volunteer donors, we experience one case among every 278 patients and about one serious or fatal case among every 1,000 patients transfused.

"Second, the use of commercial blood carries a risk of causing transfusion hepatitis that is 10 to 70 times greater than when blood from volunteer donors is used.

"Third, it is not possible in most instances for the doctor to know if the blood his patient is about to receive is from a high or low risk population."

Then if we can go to the next column please, Paul, his sixth point:

"90 per cent of post transfusion hepatitis from blood can be traced to the use of commercial or prison

blood. The elimination of the use of these donors would be of most help to reduce transfusion hepatitis to a minimum, until a test of greater accuracy can be developed to detect the infectious carrier. We cannot develop a reliable national all-volunteer blood programme [you see this is in the States] as long as blood insurance programmes are permitted to exist or as long as commercial blood is part of a blood bank operation functioning under the euphemism of not for profit. This is an important matter to the patient's health."

Still in 1971, could we go to DHSC0002173_048, please. This is a report that was prepared for an April 1971 meeting of haemophilia centre directors. We will be coming back, sir, to documentation relating to haemophilia centre directors many times over the coming weeks as we hear witness evidence from clinicians. For present purposes I'll just look at the first page. We'll see it's entitled:

"Jaundice and Factor VIII antibodies in treated patients with haemophilia and Christmas disease. At a meeting of the directors of the 36 haemophilia centres of Great Britain held in 1967 it was decided to make a study of the incidence of transfusion hepatitis and inhibitors, two most alarming

complications of treatment of patient with coagulation defects."

Reference is made to forms having been prepared and which clinicians were invited to report the incidence of jaundice. Then the next paragraph reads:

"Transfusion hepatitis is thought to be a virus infection transmitted to the recipient by the donor plasma. There is every reason to suppose that the virus is contained in the various protein fractions used to treat haemophilia and Christmas disease, cryoprecipitate, human antihaemophilic globulin or HAHG and factor IX concentrate."

Then this:

"The danger of infection can be calculated and will be related to the number of donors used to make the material used for treatment or the number of donor exposures. If large pools of plasma are used to make therapeutic concentrates the theoretical danger of infection will be increased."

As I say, it's a document we will come back to at a later stage of the hearing so I will leave that document there.

Move to 1972 back to the States. Could we have please, Paul, DHSC0100024_079. In March of 1972 in the States, President Nixon directed the Department of

Health, Education and Welfare to study and recommend a safe, fast and efficient nationwide blood collection and distribution system. It's there recorded that:

"Authorities in the health field regarded the present system as inadequate, pointing out that hospitals in many cases are forced to buy blood from commercial blood banks, which often accept blood from such donors as derelicts and drug addicts who may be the transmitters of such diseases as hepatitis, syphilis and malaria."

There's another report, I don't ask you to put it up, Paul, but in case anyone is interested in reading further on this, Nixon's announcement is also described in RLIT000223.

SIR BRIAN LANGSTAFF: Just before you leave that document, this is not just an extract from an American publication which stays, as it were, in American readership, because it seems the original of this was sent to the CMO.

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: The CMO is now returning this for the files.

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: So some time very shortly after President Nixon said what he said about the dangers of

blood, the CMO here saw it.

MS RICHARDS: Yes, absolutely, sir. This is a Department of Health document and you are right we see from the bottom original returned to CMO (Chief Medical Officer) 29 March 1972.

Could we then have please, Paul, RLIT0000169. This is an article by Dr Maycock whose name we've seen now a number of times of the Blood Products Laboratory in Elstree. It is headed "Hepatitis in transfusion services". There are just two passages we'll look at.

The first is the first part of it:

"The transmission of viral hepatitis is the most serious complication of the use of blood and blood products. Two forms of hepatitis may be transmitted in this way. One has a short incubation period of some 15 to 40 days and is generally referred to as infectious hepatitis, a disease usually transferred by the oro-faecal route and assumed to be caused by an agent known as virus A or IH virus. The other form is serum hepatitis, one of the characteristics of which is a prolonged incubation period of some 40 to 150 days, occasionally 180 days. It is assumed to be caused by an agent known as virus B or SH virus."

So we see here the nomenclature or terminology changes over the years but we see here what we

commonly now refer to as hepatitis A and hepatitis B being identified here:

"Serum hepatitis seems to occur more frequently than infectious hepatitis as a result of the administration of blood and blood products."

Then if we could go to the last page of this document, please, Paul under the heading conclusions, what Dr Maycock says there is:

"The incidence of serum hepatitis will diminish as transfusion services adopt the practice of excluding all donations of blood in which the Australia antigen is detected."

Then the next paragraph says this:

"Following the demonstration of the association between the presence of Australia antigen in transfused blood and the occurrence of hepatitis in a proportion of the recipients, terms such as 'safe blood' and 'safe blood products' were applied to blood and products derived from it in which the antigen had not been detected. At the present time both terms are misleading because treatment with blood and blood products, except immunoglobulin and albumin which has been heated [and gives the details there] continues to carry the risk, admittedly a diminished one, of transmitting hepatitis. Blood and blood products

known to be potentially icterogenic should be used with discrimination. They should be administered only when the benefits they are likely to confer upon the patient outweigh the risk to which their use exposes him."

That's the view being expressed in 1972 by Dr Maycock of the Blood Products Laboratory.

(Brief pause)

MS RICHARDS: From 1972 onwards we begin to see, in various medical and scientific publications, observations from clinicians that, even after the exclusion of donors who had tested positive for hepatitis B antigen, there were still residual cases of post-transfusion hepatitis, and so it began to dawn upon clinicians that there may be another form of hepatitis transmitted by blood or blood products other than hepatitis B.

There are a number of reports in relation to that and we will just go, for present purposes, to one of them.

Paul, it is PRSE0001431.

This is a publication in The Lancet in August of 1974 by Prince and others. It is called "Long-incubation post-transfusion hepatitis without serological evidence of exposure to hepatitis B

virus", and we can get the message from the summary:

"An agent other than hepatitis B (HB) virus seemed to be the cause of 36 (71 per cent) of 51 cases of post-transfusion hepatitis identified during prospective biweekly serological follow-up of 204 cardiovascular surgery patients. The sera of the 36 cases showed no evidence of the antigen or antibody response expected to accompany infection by HB virus and to be detectable by the sensitive assays used."

Then it refers to consideration of cytomegalovirus, and then says this:

"The data suggests that a large proportion of long-incubation post-transfusion hepatitis is unrelated to hepatitis B and that control of post-transfusion hepatitis will require identification of a hepatitis virus(es) type C."

This is, I think, probably the first reference in the medical literature to what was subsequently identified as hepatitis C.

If we go to the last page of this document, please, Paul, the first main paragraph on the left-hand side:

"The fact that non-B hepatitis cases are less frequently associated with serious acute illness does not imply that such cases are of lesser importance.

Long-term complications of acute hepatitis B infection, such as chronic hepatitis, cirrhosis and hepatoma, have been reported to follow mild anicteric infections more frequently than severe icteric cases; consideration must thus also be given to the possibility that non-B hepatitis may play a role in the aetiology of some forms of chronic liver disease."

So there again in this report, identification of the potential serious long-term consequences for the liver of this newly recognised third form of hepatitis.

SIR BRIAN LANGSTAFF: By the word "acute", we are to understand something lasting for six months or less?

MS RICHARDS: Yes. So the distinction is between, as it were, the short-term and the longer term.

SIR BRIAN LANGSTAFF: So every disease will have its acute phase but once it goes past six months it becomes known as chronic?

MS RICHARDS: Yes.

If we have, please, Paul, CGRA0000694, I think we can see that this finds its way into national publication. This is The Times for November 12, 1974:

"The Science Report: New Strain of Hepatitis Isolated."

If we just pick it up in the third paragraph:

"Two strains of virus have been known for a long time: hepatitis A (originally called infectious or short-incubation hepatitis), and hepatitis B (sometimes called post-transfusion hepatitis, because it is spread through donated serum and other blood products, and injections with contaminated needles).

"The existence of at least one other strain has been apparent during the past six or seven years because research has shown that a large number of patients, particularly those infected from transfusion or injection, were not carrying the hepatitis A or B strains. In the United States up to 50 per cent of transfusion-associated illness is caused by this third 'non-A non-B' agent."

So we see there the terminology that, over the following years, became associated with this particular virus: "non-A non-B hepatitis".

Could we then, Paul, move to CBLA0000249, please.

This is an important letter from Dr Garrott Allen, again, to Dr Maycock this time, at the Blood Products Laboratory. It's dated 6 January 1975 and Professor Garrott Allen is raising questions about the usage of Factors VIII and Factors IX, and we pick it up in the third paragraph:

"Dr Pool ..."

That's a reference to Dr Judith 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. Dr Biggs mentioned in her letter in Lancet last June 29th that there was two other commercial sources but Judy Pool did not know which they were or whether they were from the United States.

"As you know, Cutter's product Konyne for Factor IX deficiency has proved extraordinarily hazardous, a 50-90 per cent rate of icteric hepatitis developing from it. About half of these cases prove fatal. Cutter's source of blood is 100 per cent from skid row derelicts. The other imponderable which has troubled most of us is the ineffectiveness in screening for the HB antigen. This failure of course dates back to at least 1971 and suggests that half if not more of the cases of post-transfusion hepatitis are caused by an agent other than hepatitis A or B. Whatever this other agent may be, it still seems to be more frequently encountered in the lower socio-economic groups of paid and prison donors."

Then if we go to the next paragraph:

"A blood bank for these groups in the

United States is a monetoropic establishment. The commercial blood banks attract these kinds of donors. Until we understand this problem better, I would hope that Great Britain would give some thought to what the purchase of Factors VIII and IX from the United States tends to do to our attempts to form a volunteer programme. Commercial blood banking perpetuates the high risk rates for hepatitis we encounter with their products and it also tempts those same commercial firms to sell the residual products of these high-risk donors to non-immunised patients who tend to be more susceptible to post-transfusion hepatitis than is so far the non-virgin haemophiliacs."

SIR BRIAN LANGSTAFF: When he uses the word "monetotropic", he is saying it attracts money, is he?

MS RICHARDS: Yes, I assume so, sir.

SIR BRIAN LANGSTAFF: It's an unusual word but I think that's what it means.

MS RICHARDS: It is. It's not one I've ever come across and I'm afraid it's not one I looked up, so I'm going to defer to your greater knowledge --

SIR BRIAN LANGSTAFF: Well, "tropic" I think means attracting, and "moneto" sounds like a money to me. If anyone has a better definition then they can let me know in due course.

MS RICHARDS: I am sure someone sitting alongside or beside me will be online on the Oxford English Dictionary as we speak. That's a hint!

Again, for reference, I am not going to take to it but we do have Dr Maycock's reply, and for those who are interested, it's at CBLA0000254.

Can I then, and we're still in 1975 here, go to PRSE000009. This is a document that Lord Owen referred to in his evidence yesterday, which we didn't look at during his evidence. I might have missed out a zero there, Paul, sorry.

Thank you.

So it's an example of what Lord Owen referred to as a "Dear Doctor" letter, so a means by which the Chief Medical Officer might communicate advice and information to medical practitioners. This is dated 1 May 1975 to all regional medical officers. It is headed "Blood donation and hepatitis", and it is from Dr Yellowlees who was the then Chief Medical Officer. It says:

"The Department has recently received advice from a group of experts on the use of blood donations from certain categories of donors."

Various matters are then set out relating to geographical factors. I am not going to spend time on

that for present purposes but if we could go to the second page under the heading "Prisons" the letter says this:

"There is a relatively high risk of hepatitis B being transmitted by the blood of prisoners. But there is probably an equally high risk in other groups of the population, eg drug addicts, who are not so easily identified in advance as prisoners, if they can be identified at all. The advice we have received is that it is not necessary to discontinue the collection of blood at prisons and similar institutions provided all donations are subjected to one of the more sensitive tests referred to above."

We will come back when we look at a document in the '80s to the question of continuing collection of blood from prisoners in the United Kingdom.

Without again going to too many documents, there are further articles reported in the course of the mid-1970s about this newly understood and recognised hepatic virus. One example again for the benefit of those who want to look at this in more detail is a report by Alter in The Lancet in November 1975. Paul, you don't need to put it up on screen but it is PRSE0001172.

That brings us to the end of 1975 and what

I propose to do now, sir, is to play the World in Action documentary that was broadcast in two parts on 1 December 1975 and then a week later on 8 December 1975.

Many of you will have seen this and be very familiar with it but not everyone, and the broader public may not know that in 1975 this documentary was made and broadcast. It's going to provide an important backdrop for the evidence we hear from clinicians and others over the coming months.

So, Paul, could we play, please, MDIA0000113. This is part 1 of "Blood Money", the World in Action documentary broadcast on 1 December 1975.

(Blood Money, Part 1, World in Action, played)

It will eat into lunch by probably 7 or 8 minutes if we play the second half now, start lunch a little late, have the full lunch and then pick up the documents again after lunch, if that's all right?

SIR BRIAN LANGSTAFF: That would be a good idea.

MS RICHARDS: So if we could play the second part of this documentary, Paul, which is MDIA0000114.

(Blood Money, Part 2, World in Action, played)

Sir, it is 1.05. That would be a convenient point, I think, at which to break for lunch.

SIR BRIAN LANGSTAFF: We'll take a break until 2.05.

2.05, please.
(1.06 pm)
(Luncheon Adjournment)
(Luncheon Adjournment)
(2.06 pm)
SIR BRIAN LANGSTAFF: Ms Richards, can I just raise something with you which arose to me on reflection of the material you produced this morning. You produced quite a lot of material which evidences that there was a knowledge that voluntary/non-remunerated blood donors were less likely to produce an infected product than were paid donors, particularly those from the United States in the social groups from which they came.

You have established that there was material which showed that as one increased the pool size so the risk of infection within that pool from one or two donations was increased.

At the end of yesterday I asked Dr Owen what he could say about the relative pool sizes used to produce product in the NHS on the one hand and commercially on the other. In the documentary which we've just seen, there was a reference -- two references, one to the United States, where I think they quoted the figure of 2,000 to 6,000 litres of

plasma from which pools were made, and the other the NHS, 100 to 200 litres of plasma.

This is the point I want to run past you. I am raising it with you really so that if anyone from their different perspectives who's listening, from the recognised legal representatives, would wish to comment and correct me if this is a wrong deduction, one inference would be that assuming, and the assumption may be wrong but assuming, that a litre is composed of two donations, each roughly half a litre of blood, or maybe four donations, probably more likely because a litre is a couple of pints, give or take, that would mean that in the States there would have been between 8,000 and 24,000 donations, individual donations, in a pool and in the UK somewhere between 400 and 600. If my arithmetic is right. Again, it may need to be checked.

Of course, we don't know -- that's donations, it's not necessarily donors, because if the evidence produced by those who made the documentary is right, a number of those who went to give donations at the blood centres, plasma collection centres in the States, gave it repeatedly, twice a week, and may possibly have given it to more than one centre in addition. So there may have been a smaller number of

donors but that might give some idea of the relative size of pools.
MS RICHARDS: Yes. Yes, it might, sir.
SIR BRIAN LANGSTAFF: That's just what I wanted to raise, to see if those inferential figures bear that inference, and if anyone has any suggestion that they don't they can come back to you.
MS RICHARDS: Yes, thank you, sir.

Sir, the next document that we're going to look at is PRSE0004064, and it's a response from Dr Cash to the World in Action programme that we've just watched.

It's BMJ, British Medical Journal, 24 January 1976. If we could go down a bit further please, Paul, it's the letter headed "Commercial and NHS Factor VIII Concentrates". This was Dr Cash's reaction to the programme:

"One of the inevitable dangers of a journalistic approach to medical problems is that limitations in time (radio or TV) or space (newspapers or periodicals) may give rise to a selection of comments made by experts which, when taken out of context and put together for a programme or article, are misleading. This probably arose during the ITN television series World in Action."

Then he says in the second paragraph:

"There's no doubt that the import into the United Kingdom of Factor VIII concentrates derived from external sources, however well-screened for hepatitis viruses, represents an unequivocal pathway by which ..."

If we can have the top of the next column, please, Paul:

"... the level of a potentially lethal virus into the whole community is being deliberately increased."

Sir, I draw attention to that not least because of your question to Lord Owen yesterday about the concept in his evidence of deliberate decisions.

"Although the absolute magnitude of this problem is exaggerated and over-dramatised by the television programmes, nobody with direct or indirect responsibilities for this phenomenon would wish to belittle the serious nature of the moral and practical dilemma which face us all."

Then he goes on to comment specifically about the £500,000 and NHS targets, which is obviously an issue that we'll be revisiting in future hearings.

The next document, please, Paul, is HSOC0016695 -- oh, I'm so sorry, yes, HSOC0016685. I have transcribed it incorrectly in my notes.

This is an article published in July 1976 in the Journal of Laboratory and Clinical Medicine. It's by Hoofnagle and others, and the title:

"The prevalence of hepatitis B surface antigen in commercially prepared plasma products."

I just want to go to the last paragraph of the whole article, please, Paul, so the last page of the document.

Sorry, the one before that, not the list of references, the last text above that. Thank you.

So the last paragraph of the article, picking it up in the second sentence:

"Recently it has been shown that not all post-transfusion hepatitis can be classified as type B hepatitis. More startling was the finding that the non-B post-transfusion hepatitis could not be classified as type A hepatitis. This has led investigators to postulate the existence of a third human hepatitis virus, a virus which also appears to be harboured in blood. It's possible that this third hepatitis virus can withstand the pooling and fractionation procedure and that it's responsible for some cases of hepatitis following the use of high-risk plasma products. At present there are no markers and no means of detecting this virus in blood. Until the

nature of this virus and its disease is elucidated, it is important to consider human blood and pooled plasma products as potentially infectious. At the present time, fibrinogen, AHF and Factor IX concentrates remain high-risk plasma products which must be considered likely to produce overt hepatitis in susceptible recipients."

So, again, the clear recognition of non-A, non-B hepatitis there.

Paul, if we could then have CGRA0000934. If we just zoom in a little on that letter. This is another letter by Professor Dr J Garrott Allen from Stanford University. The date of this is May 1976 and you'll see it's headed "The High Cost of Cheap Blood". It's a communication to the New England Journal of Medicine and it is essentially on the same theme as we've seen from Dr Garrott Allen and indeed we saw in the programme. Just picking it up in the last -- the paragraph that's already highlighted on this copy. He's referring to recommendations made in the States from the Council on Wage and Price Stability, CWPS and says:

"They reason that because patients with haemophilia have been given transfusions they have had their hepatitis and can receive products from high

risk commercial donors. This is the same error the British made in 1974 when they augmented their supply of haemophilic concentrates with commercially prepared products form American pharmaceutical companies. Craske reported a rise from 3 to 50 per cent in case of hepatitis among his small group of patients with haemophilia. As his studies have extended, the score in late November was 58 cases, with two deaths. This hazard was predicted before it was observed."

Then please, Paul, PRSE0000381. This is an Article published in the Yale Journal of Biology and Medicine in July 1976 by Purcell, Alter and Dienstag, non-A, non-B hepatitis. If we could go to the second page please, Paul, picking it up in the second paragraph:

"The development of sensitive tests for indicators of hepatitis A virus infection now makes it possible to divide non-B hepatitis into type A hepatitis and non-A, non-B hepatitis. Although the term type C hepatitis has been suggested for the latter disease, there is evidence that non-A, non-B hepatitis may be caused by more than one agent and we believe it is wiser, therefore, to use the less mellifluous but more accurate designation non-A, non-B type hepatitis. The term type C hepatitis should be

reserved until non-A, non-B hepatitis can be defined serologically."

Hence we see non-A, non-B hepatitis as the terminology used from pretty much this time on until the late 1980s.

Then if we could go to the next page, please, Paul, picking it up in the third paragraph:

"As with type B hepatitis, type non-A, non-B hepatitis occurs significantly more frequently following transfusion of commercially derived blood than following receipt of blood derived from volunteer sources. Thus type non-A, non-B disease has been found to occur five to ten times more frequently following transfusion of the former than following transfusion of the latter."

Then the next paragraph begins:

"The epidemiology of non-A, non-B hepatitis resembles more closely that of type B hepatitis than that of type A disease."

Then if we can go to the next page, please, picking it up about halfway down:

"Although type non-A, non-B hepatitis is associated with less severe acute illness than type B disease [and again the emphasis there is upon acute, so the short-term, first six months] the long-term

prognosis for the two diseases may be similar", and then there's reference to elevated transaminase values, reference to various studies on particular patients. Then the last sentence of that paragraph:

"Thus, chronic non-A, non-B hepatitis is not necessarily a benign infection and may be the cause of a significant proportion of chronic hepatitis not identifiable as type B disease."

Could we then please, Paul, still in July 1976 go to PRSE0001579. Now the context of this document, sir, is a discussion triggered by the recommendation of the advisory group on testing for the presence of hepatitis B surface antigen, a particular recommendation to discontinue the practice of permanently excluding donors with a history of jaundice.

If we could go to the fifth page please, Paul, what we have there, the document is headed, "Comments by the Royal College of Physicians", so the Royal College of Physicians were commenting upon this recommendation and suggesting that the recommendation should not be implemented. About halfway down the page, we have a passage which says this:

"Furthermore, transfusion hepatitis may be caused by viruses other than hepatitis B for which at

present no tests are available. The existence of hepatitis C was postulated recently."

That's a comment from the Royal College of Physicians opposing the recommendation. If we look at the previous page, Paul, this is the response of the DHSS to the observations by the Royal College of Physicians. They make a number of points. I just wanted to pick up the point at paragraph 7:

"The DHSS response is no evidence has been collected yet in UK to substantiate the presence of a hepatitis C."

It may be thought there is a foreshadowing there of the mantra of no conclusive proof that we will see when we look at documentation relating to HIV.

Paul, if we could then please have PRSE0002602. This is an article in The Lancet, we're now 12 March 1977, by Dienstag, Purcell, Alter and others. If we could go to the third page please, Paul, left-hand column towards the bottom of the page if you could scroll down, we see a passage beginning:

"Besides these data other evidence for non-A, non-B [and that's the data referred to earlier in the Article. I won't go into the detail of that] other evidence for non-A, non-B agents has been accumulating. Non-A, non-B hepatitis has now been

recognised in Britain [possibly not by the Department of Health and Social Services if the previous document is accurate] in Australia, Japan, Costa Rica and possibly Germany. Not only does non-A, non-B hepatitis occur worldwide but it's apparently spread by modes other than transfusion."

Then we see a range of different routes identified including haemodialysis, renal transplant:

"Several instances of chronic hepatitis have followed acute non-A, non-B hepatitis. We feel there are adequate data to support the existence of non-A, non-B viruses."

So that's the medical and scientific perspective. Then if we go please to RLIT0000226 we see in this document that the existence of non-A, non-B hepatitis now appearing to be essentially a clinical consensus, consideration being given to the nature and seriousness of the disease. This is an article in May 1977 in Gastroenterology entitled, "Development of chronic liver disease after acute non-A, non-B post-transfusion hepatitis", by Knodell and others. Paul, if we could go to page 7. It is the penultimate page.

Under the heading "Discussion", that long paragraph towards the end of the paragraph, please,

I'll just pick it up here:

"In this study, 44 cases of acute non-A, non-B post hepatitis have been followed prospectively for development of chronic liver disease. Ten patients, 23 per cent, had persistent liver enzyme elevations from 12 to 36 months after acute transaminase elevations were first recorded. Liver biopsy specimens from these ten patients provide evidence that acute non-A, non-B hepatitis (hepatitis C?), can progress to chronic liver disease and cirrhosis."

Then if we go to the next page, top of the next page:

"The frequency with which the acute hepatitis cases caused by this non-A, non-B hepatitis-producing agent progressed to chronic liver disease was high. Histologically, eight of the ten cases of non-A, non-B chronic hepatitis had progressed to chronic active hepatitis and an additional patient already had developed cirrhosis."

Then, on the same theme, I think two further documents. RLIT0000228, please, Paul. This is in the Annals of Internal Medicine, July 1977, an article by Hoofnagle and others entitled "Transmission of non-A, non-B hepatitis."

Again, Paul, if we can go to the penultimate

page, so it is page 6 of 7. We see on the right-hand column a paragraph beginning:

"Several clinical and epidemiologic features of non-A, non-B hepatitis have become clear from studies such as the present one. First, non-A, non-B hepatitis closely resembles type B hepatitis. The incubation period, clinical symptoms and signs, and the potential for chronicity appear to be similar to type B hepatitis. Undoubtedly what was once referred to as 'serum hepatitis' included both type B and non-A, non-B hepatitis."

Then it deals with the route of transmission, spread predominantly by the parenteral route, and then third:

"Non-A, non-B hepatitis appears to be associated with a chronic carrier state and chronic liver disease."

Then skipping a few lines:

"Finally, non-A, non-B hepatitis appears to be common."

Then, Paul, if we can have PRSE0003622 this is a report in The Lancet in September of 1978 by Professor Preston, Dr Underwood, Dr Mitchell and others based in Sheffield. It's looking at the position of chronic liver disease in haemophiliacs,

and we can pick it up in the summary at the top:

"Systematic screening of 47 haemophiliacs in Sheffield revealed abnormal liver function tests in 36 (77 per cent) with a tendency for these abnormalities to persist. To assess the importance of these abnormalities, percutaneous liver biopsy was carried out on eight symptom-free patients under Factor VIII cover. A wide spectrum of chronic liver disease was demonstrated, including chronic aggressive hepatitis and cirrhosis."

Then if we could go to the third, the last page of this document, Paul, under the heading "Discussion", the second paragraph:

"We confirmed earlier observations that percutaneous liver biopsy can be carried out safely in haemophiliacs given adequate Factor VIII cover and appropriate laboratory control. As with any non-haemophiliac patient, there is a risk of haemorrhage with this procedure but experience supports the statement of Lesesne, et al, that the potential risks of complications from liver biopsy in haemophiliacs are outweighed [et cetera].

"We also found a wide spectrum of chronic liver disease, including benign self-limiting hepatitis, potentially treatable chronic aggressive hepatitis and

established cirrhosis. All our paints were symptom-free at biopsy and it was impossible to differentiate between the different forms of liver disease on the grounds of biochemical abnormalities. Since the patients undergoing biopsy had been arbitrarily selected, it is reasonable to conclude that a large proportion of haemophiliacs receiving treatment with Factor VIII have important chronic liver disease."

We will undoubtedly, sir, in the course of the evidence over the coming weeks return to Professor Preston's findings in 1978 and how others responded to them.

If we could then, Paul, go to DHSC0002191_026. This is a letter, January 1979, 8 January 1979. It's from Dr Dane the School of Pathology at the Middlesex Hospital Medical School, and it's addressed to Dr Waiter at the DHSS. It is about non-A, non-B hepatitis, and the plan was for there to be consideration of that at a meeting. I just wanted to pick up on the second paragraph:

"If one or more of these viruses is responsible for the abnormal livers which are evidently common among haemophiliacs, then chronic liver disease due to these viruses might also be found among other

transfused individuals."

So an acceptance there apparently that abnormal livers are evidently common among haemophiliacs. The reference there to Dame Sheila is to Dame Sheila Sherlock, who was then a leading expert on liver disease.

Then if we go next, please, Paul, to NHBT0000186_004. We see here a meeting invitation from the Medical Research Council. It's dated 7 February 1979. It's addressed to Dr Craske. There are similar invitations to others to attend the meeting:

"Dear Dr Craske, *ad hoc* meeting on non-A, non-B hepatitis."

It's an invitation to attend a meeting that took place on 12 February. I just draw your attention to this:

"The Chief Scientist of the Department of Health and Social Security has informed the council that this subject is being given high priority by the Department. Some batches of a commercial product containing Factor IX have been found to transmit this form of hepatitis to chimpanzees and as a result the product has not been given a licence. This is causing considerable anxiety from the point of view of the

treatment of patients. Also laboratory staff generally are beginning to enquire about laboratory safety, and trials of blood products are becoming difficult to stage because of concern over hepatitis transmission. Two aspects on which the Department sees a need for further work: research which will identify/characterise the agent carrying non-A, non-B hepatitis, and studies leading to the development of a test for the organism or its marker."

Sir, I am not going to go to the notes of the meeting itself. Again, undoubtedly it's a document that we will look at again over coming months. For those who are interested, I think it can be found at PRSE0001960.

Could we then, please, Paul, have BART0002487. This is a communication in April 1979. It's from Dr Kernoff at the Royal Free to Dr Colvin at the London Hospital.

If we just go to the last page for a moment, Paul, we can see it's written by Dr Kernoff in his capacity as Chairman of the Haemophilia Working Party of the NETR Association of Haematologists, and it's addressed, if we go back to the beginning of the letter -- sorry, Paul -- to Dr Colvin in his capacity as secretary of the NETR Association of

Haematologists.

SIR BRIAN LANGSTAFF: That's North East Thames, is it?

MS RICHARDS: Yes, North East Thames Region, yes, it would be.

If we can go to the second page please, Paul, under the heading "Two types of therapeutic material available" -- sorry, I should add, of course, that both Dr Colvin and Dr Kernoff were closely involved with the treatment of patients with bleeding disorders. So, "Types of therapeutic material available". If we pick it up halfway down that paragraph, Dr Kernoff says this to Dr Colvin:

"Not only is commercial concentrate expensive but there are both clinical and moral reasons for preferring the NHS material. The clinical reason is the growing awareness of the probability that commercial concentrates have a higher risk of transmitting non-A, non-B hepatitis than NHS material."

Then Dr Kernoff says this:

"This is a serious disease with long-term consequences which, as far as is known, is at present much less common in the UK than in those parts of the world, particularly the USA, where donor blood for commercial concentrates is collected. We may

therefore be introducing diseases which are not yet endemic in the UK. The moral reason for preferring NHS material is that it seems inappropriate to many that the maintenance of adequate standards of treatment to NHS patients should be dependent on blood obtained from paid donors from foreign countries."

But we can see there a recognition of the nature of non-A, non-B hepatitis as a serious disease with long-term consequences.

If we can then move from 1979 to 1980 and have, please, RLIT0000180. This is a study which looks at the position of children. It is from the archives of Disease in Childhood, 1980, "Liver disease, complicating severe haemophilia in childhood", by McGrath and others. Again, the research appears to be based at Sheffield Children's Hospital and Sheffield University Medical School. Summary:

"Liver biopsies were performed in 5 boys aged between 2 and 9 years with severe classical haemophilia who had persistently abnormal liver function tests. Abnormal histology was present in all; 4 had chronic persistent hepatitis and the fifth chronic aggressive hepatitis with early cirrhosis. Evidence of previous hepatitis B infection was present in one patient [et cetera, et cetera]. The

significance of these findings in young boys is discussed, as is the role of exposure to Factor VIII containing blood products. It is concluded that cryoprecipitate should be used in preference to large pool Factor VIII concentrates in children with haemophilia."

If we could go to the last page, please, and I'm grateful this was a document flagged up by representatives from one group of core participants on the basis it does look specifically at the position of children, and if we go to the bottom of the left-hand column on the last page, Paul:

"This study suggests that only brief exposure to Factor VIII concentrates (13 to 45 batches) is necessary to produce chronic liver damage in at least 25 per cent of haemophiliacs requiring regular treatment. As children usually receive treatment in hospital until considered suitable for treatment at home we recommend such patients should, if possible, be treated with cryoprecipitate in preference to large pool Factor VIII concentrates until the significance of the chronic liver damage is better understood or until such Factor VIII concentrates have been refined to exclude viral hepatitis agents."

Then there's a discussion about the use of

biopsies.

Two further documents from 1980. The first is WITN0282008 please, Paul. This is a memo, a minute, from Dr Diana Walford to Mr Harley within the Department of Health and Social Security and it's dated 15 September 1980. The context is, and we heard some allusion to this in Lord Owen's evidence yesterday, the possible commercial takeover by Beecham's of BPL. In the context of discussing that, Dr Walford said this, third paragraph:

"I must emphasise that 90 per cent of all post-transfusion and blood product infusion hepatitis in the USA and elsewhere is caused by non-A, non-B hepatitis viruses which, unlike hepatitis B, cannot at present be detected by testing donor blood. This form of hepatitis can be rapidly fatal, particularly when acquired by patients with pre-existing liver disease or can lead to progressive liver damage. It can also result in a chronic carrier state thus increasing the pool of these viruses in the community."

So an important recognition there, sir, in 1980 by Dr Walford of the DHSS of the serious nature of non-A, non-B hepatitis.

Then finally from 1980, Paul, could we have PRSE0003209, please. This is a document authored by

Dr Craske for a symposium of the Royal College of Physicians, I think. It's called, "The epidemiology of Factor VIII and IX associated hepatitis in the UK". If we could turn please to page 7, we see this being said. Under the heading, first of all, "complications", it said:

"Most cases of non-A, non-B hepatitis are mild illnesses. Six cases have been reported as severe. Two patients have died in the acute stage of the disease but there were complicating factors in both instances."

Then there's a discussion of acute fulminating hepatitis. Then discussion of chronic liver disease. There's reference to persistently elevated levels and then this:

"Most of these patients are symptomless, however a few have clinical features suggestive of chronic liver disease but the ethical problems associated with the indications for liver biopsy meant that few patients have so far undergone this procedure. About 40 patients have undergone biopsy in the UK and approximately 50 per cent of these have histological evidence of chronic persistent hepatitis. Other patients showed evidence of chronic liver disease or cirrhosis."

Then skipping down a sentence:

"The only common factor was regular treatment with Factor VIII concentrate. Most of the patients in this group are children or young adults, though the age range at Oxford is 6 to 70 years. It seems likely that some patients will develop severe chronic liver disease over the next ten years."

The reason for drawing attention to that in particular, sir, obviously is Dr Craske's close association with the Haemophilia Centre Directors organisations, the meetings of which he attended on a regular basis and to whom he gave regular advice.

SIR BRIAN LANGSTAFF: Can you just give me one moment.

Yes, I have a note just to compare what you were saying in February 1979 with what he was saying there. My note of 1979, the reference is PRSE0001960, you mentioned it earlier, that reference, where he was quoting the views, not his views but the views of what he described as American and German workers, that up to 40 per cent of non-A, non-B infections progressed to chronic liver disease and so, so far as chronic liver disease and non-A, non-B infections are concerned, that's what he seemed to be saying then.

Is he saying anything different in this article?

MS RICHARDS: I'm not sure that he is, sir. It may be

that under the heading "Complications" where he says most cases of non-A, non-B hepatitis are mild illnesses he's thinking there of the acute phase and the acute phase only, and that would make sense both of what he'd previously said and with what he then goes on to say under the heading "Chronic liver disease".

SIR BRIAN LANGSTAFF: So that might be a reconciliation of the two?

MS RICHARDS: It might be.

Paul, could we then have, please, HSOC0008581, please. This is a series of Hansard extracts from various dates. Could we go to the last page of the document, please. Here we have an extract from Hansard on 24 February 1981, so we're now in early 1981. This is Lord Cullen who is responding on behalf of the Government, that's apparent from the previous page. Lord Cullen says this:

"My Lords, blood products are not purchased centrally. They are purchased by health authorities. I regret that up-to-date information on the expenditure on imported products is not available."

It is obviously pertinent to some of the observations from the witness yesterday.

"The country from which these products come is

mainly the United States. Some also come from Austria and one or two other European countries. So far as concerns making sure that these products are free from infection, undoubtedly the careful checks which are made at all stages are extremely effective for all except a very few products, one of which is used in the case of haemophiliacs. There is a danger that Factor VIII which has to be injected into haemophiliacs can have in it a strain of hepatitis and at the moment there is no way of testing for these strains. That is the one product as to whose freedom from infection we cannot be absolutely certain. However, every effort is made to see that it is not infected and although, occasionally, something may happen, it is not of a serious nature."

That is obviously, it's fair to say, in fairly stark contrast to the material in the medical and scientific literature that we've been looking at in the second half of the '70s.

1981 of course is where we begin to pick up the first reports of what will become known as AIDS. Paul, could we please have CGRA0000242. This is the June 1981 morbidity and mortality weekly report by the Centres for Disease Control in the States and we see here under the heading, "Pneumocystis pneumonia,

Los Angeles", identification in the period October 1980 to May 1981, five young men, all active homosexuals, treated for biopsy confirmed PCP at three different hospitals in Los Angeles, California.

I won't go through all the various different MMWR reports but what we see when we trace them through is that as they continue through 1981, more and more cases are reported. So a month later, for example, in July 1981 the report is of 26 cases of Kaposi's sarcoma and a number of further cases of PCP. That continues.

If we have, please, Paul, before I return to HIV and AIDS, one further reference from this time on hepatitis, PRSE0003110. This is an article in the British Medical Journal July 1981. It is worth reading the first paragraph:

"Despite advances in screening donors and in blood fractionation post transfusion hepatitis remains the major complication of the modern treatment of haemophilia. The diagnosis is usually inferred from abnormalities in the results of hepatic biochemical tests rather than from clinical evidence. Surveys in haemophiliacs have shown changes in the liver architecture consistent with previous viral assault, including those of chronic persistent and chronic

active hepatitis and of cirrhosis."

Then this:

"Indeed, in some cases early death from liver disease might prove to be the price paid by haemophiliacs for the improved quality of life afforded by the easy availability of clotting-factor concentrates."

So the issue there addressed in the British Medical Journal, obviously a very commonly read journal for medical practitioners, in those somewhat stark terms.

If we go then please, Paul, to CGRA0000424, we are now in the CDC's morbidity and mortality weekly report for the end of August of 1981 and a significant number of further cases of Kaposi's sarcoma and PCP are reported. Third line:

"Since July 3, CDC has received reports of an additional 70 cases of these two conditions in persons without underlying disease."

Again, I'm not going to go through all of them but we then pick in December of 1981 a number of articles in the New England Journal of Medicine which considered this condition about these previously healthy individuals contracting PCP and/or Kaposi's sarcoma.

If we could then go please Paul to PRSE0004476, the second page please, this is The Lancet December 1981. So we have the articles in the States in the New England Journal of Medicine and in The Lancet a letter which is referring to the recent reports from the United States and sets out what the authors understand to be the first report of the condition in a patient in the United Kingdom a patient who had been referred to the Brompton Hospital.

We then -- I don't ask this to be turned up, Paul, but in January of 1982, because it's a rapidly developing picture, the New England Journal of Medicine reports now 159 documented cases reported to CDC between June and November. It's described as a serious public health problem with a high mortality rate.

Then throughout 1982 the MMWR from CDC continues to report an ever-increasing number of cases of KS or serious opportunistic infections.

SIR BRIAN LANGSTAFF: These are all cases generally in the community. They are not restricted to those who receive blood or blood products in any way?

MS RICHARDS: At this stage, that's correct. At this stage they are predominantly being reported in gay men and then we pick up in July of 1982 from the MMWR for

9 July reports of opportunistic infections in Kaposi's sarcoma amongst Haitians in the US, and that describes of 19 patients it says the clinical course has been severe. Ten patients have died. I will give the reference for those who want to look it up -- I won't put it up on screen -- but it's PRSE0003880.

Then same date, 9 July 1982, if we could have up on screen please, Paul, CGRA0000288. Here we see the first cases being reported in those who have received blood products. So it's a notification or a report from The Department of Health and Human Services in America to manufacturers of plasma fractionation products concerning a meeting concerning opportunistic infections in haemophilia A patients:

"Three cases of PCP in patients with haemophilia A receiving anti-haemophilic factor have recently been reported to the Centers for Disease Control. All three patients were heterosexual white men without a history of intravenous drug abuse."

Then there is reference to over the previous year the hundreds of cases of reports, most of which had been at that stage in homosexual men and individuals who were IV drug abusers. Then the last sentence of that second paragraph:

"Although the cause of this outbreak is unknown,

the information suggests that a transmissible agent might be involved and concern about transmission through blood and blood products has been raised."

So that's 9 July 1982, and we see there's a reference there to a meeting planned for the following week.

If we could then please go to PRSE0000523, Paul. We see this also being formally reported by the Centre for Disease Control in MMWR for July 16, 1982:

"CDC recently received reports of three cases of PCP among patients with haemophilia A and without other underlying disease. Two have died. One remains critically ill ...", et cetera.

Details are given of those patients.

Then if we go to the second page, please, under the heading "Editorial note", second paragraph:

"The clinical and immunologic features these three patients share are strikingly similar to those recently observed among certain individuals from the following groups ..."

Then the groups are there set out: homosexual males, IV drug users, et cetera.

"Although the cause of the severe immune dysfunction is unknown, the occurrence among three haemophiliac cases suggests the possible transmission

of an agent through blood products."

We see that this is immediately known to the Department of Health and Social Security, and we can see that from DHSC0002219_009. This is an internal DHSS minute. The date is 16 July 1982. It's not a 100 per cent accurate account but we see why when we look at the document. It's addressed to a Dr Holgate:

"Dr Holgate.

"American Factor VIII.

"You will wish to know that Dr Harold Gunson, our consultant adviser in blood transfusion, has received information from the American Bureau of Biologics via Dr Joe Smith at NIBSC that there may be considerable publicity in the next couple of weeks concerning the safety of American Factor VIII. Please forgive the layman's explanation below ..."

This is where it's not entirely accurate but the essential message is clear:

"I hope it makes some sense. Apparently, some research is about to be published showing fairly conclusively that plasma taken from homosexual drug takers contains a sort of virus which goes undetected when the plasma is tested because it is suppressed by the drugs. However, when used for Factor VIII it becomes active again. It seems that 400 haemophiliacs

in the USA have exhibited signs of the virus."

I don't think that is in fact accurate at that point in time.

"The report is expected to be picked up by the lay press and may cause a furore. I do not know which brands of Factor VIII are involved. From the DHSS point of view, we can defend the National Blood Transfusion Services' own record. Someone taking drugs, gay or not, would not be bled provided that the injection marks showed. In any case, with our voluntary unpaid donor system we do not have the same problem as in the States where drug addicts are tempted to give blood simply for the money. However, about half of the Factor VIII bought from commercial companies is imported from the USA. Your division, when the published study is available (I understand that 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 that none of the Factor VIII involved is supplied to this country."

Of course that was not the case. But we can see that at the same time as this information is being published in the States it's being shared with the Department of Health and Social Security in the way

that we see there.

If we then have, please, Paul, BAYP0004205. It's not the most legible of documents but we will see from the title it is "Summary report on open meeting of PHS committee on opportunistic infections in patients with haemophilia".

So it is a report of a meeting in the States which took place on 27 July 1982 considering the significance of the occurrence of opportunistic infections in PCP in those three patients with haemophilia. Wide variety of organisations and participants.

Then if we go to the second half of that page, under the heading "Aspects of discussion":

"AIDS [it's one of the first examples of the term being used] and the sequelae of KS and OI [that's the Kaposi's sarcoma and opportunistic infections] are occurring in several populations [they are then identified]. The possibility exists that it is incurring in patients with haemophilia. If the PCP observed in three patients with haemophilia represents the same process as seen in other groups with AIDS, then a possible mode of transmission is via blood products, in this case Factor VIII concentrate. This finding would strengthen the existing hypothesis that

AIDS is caused by a transmissible agent."

Then if we go next, please, to PRSE0003247 we move here from the States to an international congress in Budapest for the International Society of Haematology and the International Society of Blood Transfusion. It was attended by Dr Peter Foster of the PFC in Edinburgh in August 1982, and this is his report.

If we go to the last page, please, Paul, the last page with any text on -- most of the paper is concerned with a very detailed technical discussion of issues relating to fractionation and other matters. But then he makes this reference:

"In discussion future problems in the treatment of haemophilia, Aledort reported that the most recent problem to surface in the USA has been three deaths from pulmonary infections. This has been linked with the development of acquired immunodeficiency syndrome."

So this information about the three haemophiliacs in the US is clearly by this stage being widely disseminated to knowledgeable individuals.

Could we then have please, Paul, probably the last document before the break, RLIT0000200. This is an article in the publication Science,

a long-established journal. This article is dated 13 August 1982, headed, "New disease baffles medical community".

If we look in the first -- the left-hand column towards the bottom of the page it says this:

"Although other explanations have not been ruled out, most investigators currently think that the disease is caused by an infectious agent, possibly a new virus or a new variant of an existing virus. The spread of AIDS resembles that of hepatitis B virus."

Then if we could go to the next column, please, Paul, a bit further up, this is picking it up a couple of paragraphs in:

"Hepatitis B is also transmitted through transfusion of whole blood or blood products. Recently three individuals with haemophilia have come down with AIDS, an occurrence which is particularly disturbing because of the possibility they acquired an infectious agent from the blood product they take to prevent bleeding. So far, however, there is no evidence linking ordinary blood transfusions to the immunodeficiency disease ..."

Then the person cited there is a representative of the Centers for Disease Control.

Sir, I note the time. I can probably just about fit in another document or we could break and resume after the break.

SIR BRIAN LANGSTAFF: The only other thing just I note from a quick glance at what is said there in Science is if one looks at the third column across, about halfway down, it notes that the infections seen in AIDS patients which first began to be noticed in about mid-1979. Well, if that is correct, then it would look as though back in 1979, two years before the MMWR reported it in June of '81 there were developing infections and it might suggest, might it, a long incubation period?

MS RICHARDS: Yes, absolutely.

SIR BRIAN LANGSTAFF: For AIDS, from whatever was causing it.

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: We will take a break until 3.45.

(3.01 pm)

(A short break)

(3.43 pm)

MS RICHARDS: We pick the picture up in September 1982 now, HCDO0000410. This is a meeting of the Haemophilia Reference Centre directors on 6 September 1982, and it's the first reference in any

of their meetings to the question of AIDS.

If we could go please, Paul, to page 11, we'll see the second paragraph and this is how it comes up:

"Professor Bloom asked Dr Craske if he had any information about the acquired immune deficiency syndrome following reports from the United States and the possible relationship of the syndrome with blood products and hepatitis. Dr Craske said he would find out more about this and agreed to try and have some information available for the Haemophilia Centre directors at the Manchester meeting."

That Manchester meeting took place a week later. That's CBLA0001619. So we can see this is the bigger meeting, involving all of the Haemophilia Centre directors and not just the directors of the reference centres, 13 September 1982. If you could go please, Paul, to page 10, we will see Dr Craske's report back at the bottom of the page:

"The Acquired Immune 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. Dr Craske asked the

directors to let him know if they had any cases of the syndrome. The Working Party [that's the hepatitis working party of the Haemophilia Centre Directors Organisation] was considering the implications of the reports in the USA."

Sir, obviously one of the many issues that you will have to consider in due course about the response of haemophilia directors is whether this was, at this stage, a sufficiently urgent and accurate appreciation, this characterisation of a "remote possibility" of the involvement of commercial blood products.

Paul, could we have OXUH0002848, please. This is a further MMWR report from CDC, 24 September 1982. It includes now a case definition for AIDS. But for present purposes if we could just look at the third page, please, Paul, first main paragraph:

"Two points in this update deserve emphasis. First, the eventual case-mortality rate of AIDS a few years after diagnosis may be far greater than the 41 per cent overall case-mortality rate noted above."

I just draw attention to that, sir, to indicate that at this stage one thing that was seemingly apparent was the very high mortality rate from AIDS.

Paul, could we next have, please, MDIA0000010.

MDIA0000010. So we're now in the mainstream media. Rather than scientific journals or medical journals, this is The Observer, 14 November 1982. "No defence against gay disease" is the heading. If we look -- it's quite small print -- in the fourth column please, Paul, top half of the page -- fourth column:

"AIDS is not infectious though as colds and measles might be. Close relatives and friends do not catch it. A major speculation is that the AIDS virus is carried in the blood and transmitted directly either sexually or through syringes, which is how hepatitis B, to which homosexuals are also prone, spreads. This link with hepatitis might also explain the presence of AIDS among heterosexuals who inject drugs [et cetera, et cetera]. This could also explain the presence of AIDS in a small group of heterosexual haemophiliacs who injected themselves frequently with a blood concentrate designed to encourage clotting."

So The Observer there reporting in November 1982 the potential connection between -- or the potential blood transmission route of the AIDS virus.

Could we then, please, Paul, have BYAP0000018_119.

This is a new letter from the American National Hemophilia Foundation. The date is December 9, 1982.

It's concerned with AIDS, "AIDS update":

"In July of 1982 the CDC reported three cases of AIDS identified among haemophilia A patients. Since then none of these have survived. The following is a summary of a December 10, 1982 CDC update on AIDS. The CDC has confirmed four additional and one highly suspect case among haemophilia A patients."

There's reference to there being no suggestion of the haemophiliacs acquiring the disease through contact with each other or other groups known to be at increased risk.

"The MMWR points out at all of these cases to be supposed to Factor VIII concentrates and all but one have also received other blood components."

Then, if we go to the next page, please, Paul:

"CDC recommends that patients should be advised of this risk."

Then the last two paragraphs:

"It is important to note that while there is insufficient data to directly link the spread of AIDS to concentrate, there is an increased concern that AIDS may be transmitted through blood products. It is the NHF's point of view that patients and parents should be aware of the potential risks."

Then it is suggested:

"If you have any questions they should be directed to the treating clinician."

So that's the advice emanating from the States in December 1982.

If we then please, Paul, go to PRSE0003276 and if we could go please to page 4, this is 10 December 1992 MMWR. This is the report of what's referred to elsewhere as the San Francisco baby case, sir. Possible transfusion associated acquired immunodeficiency syndrome, California.

"CDC has received a report of a 20 month old infant in the San Francisco area who developed unexplained cellular immunodeficiency and opportunistic infection. This occurred after multiple transfusions including a transfusion of platelets derived from the blood of a male subsequently found to have AIDS."

If we go to the next page please, Paul, editorial note, just over halfway down the page:

"The aetiology of AIDS remains unknown but it is reported occurrence among homosexual men, intravenous drug users and persons with haemophilia A suggests it may be caused by an infectious agent transmitted sexually or through exposure to blood or blood products. If the infant's illness described in this

report is AIDS it's occurrence following receipt of blood products from a known AIDS case adds support to the infectious agent hypothesis."

We see there and if we go to PRSE0002436 this is another newsletter from the National Haemophilia Foundation in the States, the date now December 21, 1982. If we go further down we will see in the second paragraph:

"There's an increased concern that AIDS may be transmitted through blood products. Patients and parents should be aware of the potential risks. There is no conclusive evidence that cryoprecipitate or fresh frozen plasma will reduce the risk of AIDS. We feel however that this is no time to introduce concentrates to patients who have never used them before, except when there is an overriding medical indication."

Then examples of patients who should not be introduced to the concentrates at this time: new born infants through age 4, newly diagnosed cases of haemophilia, and those with mild disease.

Then it continues:

"At this time the NHF AIDS task force does not recommend a change in treatment to those who have received concentrates and therapy and by all means one

should not withhold the use of clotting factor therapy when needed."

If we then please, Paul, have CGRA0000434. This is a Cutter memo, still in December 1982. This is 29 December 1982, so pharmaceutical company:

"It appears to me to be advisable to include an AIDS warning in our literature for Factor IX and Factor VIII. I realise that very little is known about AIDS and the relationship that products we manufacture have in causing the syndrome. However, litigation is inevitable and we must demonstrate diligence in passing along whatever we do know to the physicians who prescribe the product", and then there were steps set out for inclusion in package insert, et cetera, once the wording is agreed.

So we've looked at -- sir, what Cutter was saying. We've looked at what the National Haemophilia Foundation in the States is saying. We're now going to look at the domestic Haemophilia Society, the UK Haemophilia Society. It's first bulletin of 1983. It is PRSE --

SIR BRIAN LANGSTAFF: Before you go to 1983, you mentioned a moment or two ago by reference to CBLA0001619, I think suggesting that Craske had made a report and the conclusion was that it was a remote possibility

that commercial blood products were involved and you suggested I might have to resolve whether that was a sufficient response. I don't know if we have a copy, if Paul has a copy of BPLL0011645.

MS RICHARDS: I'm not sure that he will, sir.

SIR BRIAN LANGSTAFF: Let me tell you what my note says. It will need to be checked, but I have a note that on 5 November 1982 Craske wrote a memo in respect of AIDS, so this is only --

MS RICHARDS: We do have it, sir, with a different reference, CBLA0001653_003 is Dr Craske on 5 November.

SIR BRIAN LANGSTAFF: I think he looks at the possible cause. He puts forward three possible causes and he discounts the first two causes. That is the use of amyl nitrate as a sexual heightener during homosexual intercourse and the immunosupressive effects of CMV, cytomegalovirus, which leaves only one.

MS RICHARDS: Yes, if we go to the next page, please, Paul, we can see. Yes, it's put here by Dr Craske:

"The association with sexual promiscuity, intravenous drug abuse and possibly [again, the word is 'possibility'] the transfusion of commercial blood concentrates, together with evidence of clustering and a prodromal phase, suggest an infectious agent with a similar epidemiology to that of hepatitis B."

Then he says --

SIR BRIAN LANGSTAFF: So he discounts (2) and is left with the infectious agent idea, doesn't he?

MS RICHARDS: Yes. Then he says:

"If (3) is the most likely cause ..."

Then he talks about the possibility of it being present in plasma used to prepare hepatitis B vaccines.

SIR BRIAN LANGSTAFF: I think, if you just scroll down to the end -- I don't think there's anything else there. But at least it may set the record straight so far as he is concerned. Perhaps. Something I will have to consider, in any event.

MS RICHARDS: Yes.

So, Paul, if we have, please, now -- we're in early 1983 -- PRSE0004120, please.

This is a Haemophilia Society bulletin. We don't have the precise dates, sir. It is the first bulletin that was the published in 1983 and so the date that has been ascribed on our systems in the chronology is effectively 1 January 1983. It almost certainly was later than that but we don't know the precise date.

If we could go to the penultimate page, please, Paul.

What we have towards the bottom human right corner is, if we scroll down:

"AIDS and haemophilia; an interview with Dr Peter Kernoff, director of the Haemophilia Centre at the Royal Free Hospital in London."

Then if we go to the next page, please, it's a written question and answer. I'll just refer to three of the questions and answers:

"What's the cause of AIDS?

"That's not known, but because there are similarities between the groups of people who seem to be getting AIDS and those who are known to be at risk of hepatitis B, it's been suggested that AIDS might be caused by an infectious agent, perhaps a virus, which is transmitted in the same way as hepatitis B. That is, mainly by injected blood or blood products and sexual contact. However, this is just a guess and there are several other possibilities."

He doesn't set out what those possibilities are.

"Question: I begin to see links with haemophilia.

"Answer: Yes, but they are very tenuous. Certainly we know that haemophiliacs are at higher than normal risk of getting hepatitis B because of their frequent exposure to infusions of blood

products. If AIDS is caused by an infectious agent and if this agent is transmitted by blood product infusion, and these are both big ifs, then it may be that haemophiliacs could be at increased risk of AIDS."

Then the question:

"Well, do haemophiliacs get AIDS?

"Amongst the group of patients with AIDS who have been reported to the American authorities, there have been 11 haemophiliacs. It's not entirely clear how many of these haemophiliacs had risk factors which were unrelated to their haemophilia."

Pausing there, the information in the MMWRs doesn't suggest any association with any other risk factors in its report of cases, and then the question:

"Could British haemophiliacs get AIDS?

"Of course it's possible, but I'd expect AIDS to remain a rare disease. The idea that there's an epidemic of AIDS amongst haemophiliacs is ludicrous."

Is his answer.

Paul, if we could then have CGRA0000301, please.

This is 4 January 1983. It's a report on a CDC multi-agency meeting, so it's, again, an American meeting.

If we go to the second page, the meeting that

took place in Atlanta, and if we go down to the second half of the page, "Aspects of discussion":

"AIDS continues to be a major public health problem. In addition to the previously described high-risk groups [and those are then listed] persons with haemophilia are also at increased risk of developing AIDS, presumably by introduction of a transmissible agent in Factor VIII concentrate. Five cases of AIDS have been reported in persons with haemophilia since the three described in July and two to three more are considered to be possible cases. One case of AIDS has occurred in an infant who received a platelet transfusion from a man who subsequently was diagnosed as an AIDS patient."

That's probably a reference to the San Francisco baby case.

"Several other AIDS cases under investigation [5] have no risk factors but have received blood products within the past two years. Some participants were reluctant to accept the hypothesis that AIDS has been transmitted by whole blood in the absence of additional evidence."

So that's the CDC meeting in January 1983.

Then if we could, please, Paul, have RLIT0000233.

This is a publication in Science Journal, 7 January 1983, "Spread of AIDS sparks new health concern". Picking it up in the left-hand column:

"The relentless new disease called AIDS continues to spread."

Reference to certain data, and then the second paragraph says this:

"Moreover, blood products have come under increased suspicion as vehicles for spreading AIDS. An infant who received several infusions of whole blood in blood products developed the condition. One of the donors who had appeared well at the time he gave blood eventually died of the disease. The CDC also reports the diagnosis of AIDS in four haemophiliacs in addition to the three previously identified, confirming earlier suggestions that these individuals might be at high risk."

We see here the comment from CDC, perhaps in contrast to Dr Kernoff's comment:

"'The problem in haemophiliacs is real,' says the CDC's Harold Jaffe, 'It isn't going to go away.' Their latest reports support the hypothesis that AIDS is caused by an infectious agent, possibly a virus, that can be transmitted by close contact, including that between family members, or by blood products.

The latter possibility raises a serious health issue about the safety of the blood products used by haemophiliacs and perhaps by the general public."

Then if we could, Paul, go to PRSE0002410, we are here in the New England Journal of Medicine, 13 January 1983. The article is entitled "AIDS and preventive treatment in haemophilia". If we could go to the second page please, Paul, to the last paragraph:

"The fact that haemophiliacs are at risk for AIDS is becoming clear. If the use of cryoprecipitate will minimise this risk, the current home infusion programme needs to be revised."

Then there's reference to the studies there being small studies.

"Unfortunately the data are consistent with a greater potential for AIDS in the population treated with concentrates. Physicians involved in the care of haemophiliacs must now be alert to this risk. Preventing the complications of the present treatment may have to take precedence over preventing the complications of haemophilia itself."

Then, Paul, if we could have DHSC0002223_085. Do you have that? DHSC0002223_085. Thank you.

So we're again back into the mainstream media,

the Observer, 16 January 1983, "Mystery disease threat":

"A commercial blood product imported into Britain from the US may pose a grave threat to the health of haemophiliacs, who inject it to encourage clotting."

Skip a paragraph:

"Officials at the Government Centre for Disease Control in Atlanta, Georgia, have described the spread of the disease as an impending epidemic among haemophiliacs."

Then the right-hand column, second paragraph, few lines down:

"In the past ten months the disease has spread from the homosexual community to include haemophiliacs [and various others listed]. The cause remains baffling. One theory is that an infectious agent is transmitted directly, either sexually or through contaminated blood products, in a similar manner to hepatitis B, to which homosexuals and haemophiliacs are also prone."

Then if we just scroll out, please, so we see the whole document, Paul, we can see from the handwritten notes at the top of the page that this is a document that came to the attention of the

Department of Health and Social Security, because there's a note to Dr Walford, saying to her:

"It would be useful to know the outcome of Haemophilia Centre directors meeting. Perhaps we can discuss at an opportune moment."

She's says she's written to Professor Bloom for details of the meeting. We may look at that correspondence tomorrow when we look at Professor Bloom.

So that's 16 January 1983. We then, please, Paul, could we have SBTS0000315_021.

This is an article that doesn't really say anything different from what we have seen, but the point here is this is The Lancet, so the news is being broadcast now in The Lancet, 22 January 1983, under the heading, "Acquired immunodeficiency syndrome". At the very bottom of the page:

"There are at least four major populations at risk in the USA, about 75 per cent of patients are homosexual males [if we scroll down please, Paul] 13 per cent are intravenous drug abusers with no history of homosexuality, 6 per cent are Haitian immigrants who are not homosexual and do not abuse drugs, 0.7 per cent are haemophiliacs, about 5 per cent of no apparent risk factors."

Then if we look down in the left-hand column towards the end the second long paragraph, it says:

"Finally, the syndrome may well be transmissible, women may acquire AIDS from their male partners and the disease is developed in haemophiliacs after Factor VIII administration, in a child after blood transfusion, and in four infants whose mothers either had or were at risk of AIDS."

Next paragraph:

"The overall mortality from AIDS is an alarming 40 per cent and in reality it may be considerably greater since many patients who recover initially die subsequently from malignant disease or overwhelming infection. There are few reports of complete remission."

That's picked up then in the New Scientist a few days later, PRSE0000726. You may recall we looked at this article during the evidence of Andrew Evans last year when he had a recollection of his father seeing this, "AIDS transfusion patients may be at risk", so this is the New Scientist for 3 February 1983:

"American scientists are scouring the country for the first case of the bizarre new disease AIDS in patients who have undergone major surgery."

Then skipping over a couple of paragraphs it

refers to:

"A task-force under Dr Harold Jaffe at the CDC in Atlanta has found seven cases of AIDS amongst haemophiliacs who do not fall into any of the other categories. Jaffe believes that the spread of the disease may be connected with new preparations of Factor VIII concentrate, the blood-clotting agent given to haemophiliacs which are made up from blood from large numbers of donors, rather than one individual. If this is correct, any patient in hospital who is given a blood transfusion could be at risk if one of the donors of the blood carries the virus. No cases of AIDS among British haemophiliacs have been reported so far, even though 50 per cent of the Factor VIII used in Britain comes from the US."

Sir, shortly before that article, there was a meeting on 24 January 1983 at a London airport hotel. We're going to look at two documents that relate to that meeting. The first is at RFLT0000050, so you will see this is a letter being sent by Mr Berry the managing director of Immuno to Dr Kernoff, co-director of the Royal Free Hospital -- the Haemophilia Centre at the Royal Free hospital and it was Dr Kernoff who some time after this gave the interview in the Haemophilia Society bulletin.

This is Mr Berry sending a summary of discussions at the meeting held at the Excelsior Hotel Heathrow Airport on Monday 24 January 1983. We have two accounts of this meeting. This is Mr Berry of Immuno's account and this is a document we're highly likely to come back to a number of times over the coming months, sir.

We'll see at the top of the second page:

"Summary of discussions of the meeting held at Excelsior Hotel, Heathrow Airport, Professor Bloom in the chair", and then there is a discussion, and I'm not going to go into the details of this part of the discussion about non-A, non-B hepatitis.

If we could go to the last page of this note, paragraph 13, this is the only reference to AIDS in this note and it says this:

"The possibility of reducing the risk of AIDS was not known at this stage. In any case, it is not known if AIDS is caused by a virus or an attacker inimical to T cells."

For a more detailed understanding of what discussions took place at that hotel meeting we have to go to notes made we think by Dr Bolton and that is at PRSE0002647.

Paul, could we go to the last page, first of

all, so we can see the list of attendees. Those present included Dr Evans, Manchester; Dr Barrowcliff; Dr Rizza, Oxford; Dr Hamilton, Newcastle; Dr Ludlam, Edinburgh, Dr Colvin, London Hospital; Professor Hardisty we know from Great Ormond Street; Dr Preston, Sheffield, I think I'm sure I will get some of this wrong; Dr Mayne, Belfast; we have Dr Davidson; Dr Aronstam, who was Treloars; Dr Hill, we know Birmingham; Dr Edgecombe; Dr Prentice; Dr Savage, he was St Thomas'; Dr Kernoff, Royal Free; Dr Leslie; Dr Winfield; Dr Wensley, Dr Mibashan; Dr Craske; and then we have Professor Zuckermann, who we saw in the World in Action documentary, the hepatitis expert; Dr Bloom; Dr Shinton; the Immuno team are led by Dr Eibl.

So it was a meeting involving a number of Haemophilia Reference Centre directors, others with a particular interest in hepatitis and representatives of Immuno.

Again, I'm not going to deal with the discussion about non-A, non-B hepatitis. We'll come back to that at another time but if we go to the previous page please, Paul, we see a much more detailed account than we saw in Mr Berry's note of the discussion that took place about AIDS at that January '83 meeting:

"Acquired immunodeficiency syndrome. This was discussed in the after lunch period. Dr Craske summarised the current position. He gave a clinical description of the AIDS syndrome ..."

If we go down a couple of paragraphs:

"Up to 10 December 1982 some 800 people have been reported as suffering from the AIDS and there was a 45 per cent mortality. Ten haemophiliacs in the US have been affected and five have died. The youngest was aged 7. All cases have had prolonged treatment with Factor VIII, but there is no specific implication of one particular product or batch. Other cases involving blood and blood product transmission have included platelets transfused in three cases. In one of these cases one of the donors was a young New York man in his twenties. A second case was a 20-month old child with rhesus HDN who had received several units, including platelets known to have come from a homosexual donor who was asymptomatic at the time but who later died."

That again is no doubt a reference to the San Francisco baby case:

"The child had developed autoimmune haemolytic anaemia and a possible AIDS state."

Over the page:

"The incubation period for the syndrome appears to be six months to two years. In the UK so far only one or two cases have been reported from the Communicable Diseases Centre. The infectious precautions including discouraging homosexuals from donating blood or organs. Protocols from the US are being considered by the hepatitis working party in the UK. Apparently, the American fractionation companies are very aware of the problem and are taking some unspecified measures to screen out such donors. The attention of the meeting was then drawn to the two articles on the editorial in the New England Journal of Medicine of 13 January, which in summary indicates that the T4/T8 ratios among haemophiliacs receiving Factor VIII is greater among those who have been exposed to concentrates than those exposed to cryoprecipitate only. However cryoprecipitate in the US comes from volunteer unpaid donors and therefore are presumably well motivated people. Final comments on the possible nature of the transmissible agents indicated that there may not be just one agent but a mixture, i.e. a barrage of viruses, including hepatitis B, non-A, non-B, CMV and many others possibly transmitted from asymptomatic healthy blood donors."

So a much more detailed account there of a discussion about current up-to-date information of numbers affected in the US and again, sir, no doubt we'll come back with individual witnesses to their recollection and understanding of that meeting and its significance in terms of what was done or not done subsequently.

SIR BRIAN LANGSTAFF: Is there anything else in that document which suggests anything other than some form of infectious agent or agents?

MS RICHARDS: No, sir.

That was 24 January. The next Reference Centre Director meeting, of haemophilia centre directors, was on 14 February and we'll just briefly look at that please. It is HCDO0000411. If we go to the second page please, Paul, we can see these are draft minutes but I don't think we have a final version. Minutes of the 16th meeting of haemophilia reference centre directors held at the Royal Free Hospital on Monday 14 February and we see the names of those attending almost all of whom had been at the London airport meeting approximately three weeks before.

If we look and see what was discussed about AIDS, it's the fifth page of the document, Paul. Thank you. Six lines down:

"The AIDS syndrome, Professor Bloom said that the syndrome would be discussed at the Stockholm meeting of the World Federation of Haemophilia. Reports from the United States indicated that the incidence of AIDS was higher than at first thought and there was some concern that the haemophiliac population of the UK who had received American concentrates might be at risk. Dr Craske summarised the latest information from the United States, said that approximately 10 cases of AIDS were thought to have occurred in non-haemophiliacs in London, one in Glasgow, and one in Manchester. Dr Craske had drawn up a draft form for reporting of the cases. There was a lengthy discussion regarding the report form and which of the various documents which Dr Craske had obtained from the United States should be circulated to the haemophilia centre directors. It was agreed that Dr Craske should draw up a new form for the reporting of cases and to arrange for this to be circulated to all haemophilias centre directors with appropriate notes regarding the criteria on which the diagnosis should be based. It was suggested that Dr Craske should invite an immunologist to join the hepatitis working party in view of the working party's involvement with the AIDS syndrome."

That's the extent of the discussion on 14 February. You can see the action taken there is as regards reporting and sharing of some information about diagnosis.

There is no discussion recorded in the notes of any steps to be taken to inform patients of the risk, in contrast to what we see from the National Haemophilia Foundation in the States, and no discussion recorded in the notes about any changes or possible changes to treatment policies or approaches.

Paul, if we could then please have PRSE0000546. This is now the early March 1983, 4 March. It's another MMWR report from the CDC in the States. If we look at the third paragraph:

"The distribution of AIDS cases parallels that of hepatitis B virus infection, which is transmitted sexually and parenterally. Blood products or blood appear responsible for AIDS amongst haemophilia patients who require clotting factor replacement. The likelihood of blood transmission is supported by the occurrence of AIDS among IV drug abusers."

Then reference to:

"Sharing of contaminated needles, to an infant developing severe immune deficiency and opportunistic infection [that's the San Francisco baby case again]

the possibility of acquiring AIDS through blood components or blood is further suggested by several cases in persons with no known risk factors who have received blood products or blood within three years of AIDS diagnosis. These cases are currently under investigation."

So, sir, again picking up on one of your earlier observations, no suggestion of any other cause and here the term used is "likelihood" not "possibility" of blood transmission.

If we could go to the second page, please, Paul, picked it up six lines down:

"Furthermore, the California cluster investigation and other epidemiologic findings suggest a latent period of several months to two years between exposure and recognisable clinical illness and imply that transmissibility may precede recognisable illness."

So we're there in early March. There's some relevant communications in March between Bruce Evert in the States and Professor Bloom, but I am going to deal with that when we look at Professor Bloom and Cardiff tomorrow.

Could we then please, Paul, have PRSE0000728. This is a meeting on 22 March 1983 in Scotland,

meeting of the Haemophilia and Blood Transfusion Working Group. We can see there the attendees include Dr McDonald, Dr Cash, Dr Forbes, Dr Foster, and Dr Ludlam.

If we turn please to the second page, bottom of the page:

"AIDS. Members were reminded of the recent articles both at home and abroad about AIDS. Dr Ludlam reported that in the UK a letter and questionnaire had been sent out to haemophilia directors."

That's no doubt a reference to Dr Craske's proposals which had been discussed at the February reference centre directors meeting.

"AIDS was an emotive issue in the USA and Canada and was causing a move away from the Factor VIII concentrates to the use of cryoprecipitate, with the resultant supply problems. There was concern that AIDS might appear in the UK and the Haemophilia Society was attempting to reassure its members and put fears of infection from blood products into perspective."

Next page:

"The transfusion directors were loath to ask questions to which exception could be taken by

potential donors, but it was hoped that homosexuals and others at risk might be discouraged from being donors. In the meantime the transfusion directors were considering how best to ensure the safety of the plasma supply and Dr Forbes was conducting a sample study of the immunological status of haemophilia patients. The Chairman agreed to keep the matter in view and bring it up for discussion at the next meeting."

Sir, March 1983, there was an important decision in the States.

Paul, could we have DHSC0001203.

This is 24 March 1983, a decision of the FDA, the Food and Drug Administration.

This communication is from the director, Office of Biologics, National Centre for Drugs and Biologics, to all licensed manufacturers of plasma derivatives:

"Extensive discussions among licensed manufacturers at the Office of biologics and concerned groups such as the National Haemophilia Foundation have led to a consensus concerning an appropriate approach to decreasing the potential risk of transmitting AIDS by certain plasma derivatives. Plasma collected from donors suspected of being at increased risk of transmitting AIDS [and then they are

then defined] should not be fractionated into derivatives already known to have a risk of transmitting infectious diseases."

Then if we skip down to the next paragraph:

"We request that you immediately institute procedures with your plasma suppliers to assure that they have adopted appropriate donor screening practices and procedures."

How that edict from the FDA was then responded to and played out in this country, in particular in decision-making by the Department of Health and Social Security will be something that we will explore in some detail with witnesses next year when we hear from Government witnesses.

Then if we could then have, and this I think is probably the last reference for today, it's four minutes or so from a documentary. So we're now in April of 1983 and a documentary, Horizon documentary, called "Killer in the Village" was broadcast on the BBC on 25 April 1983. We only need a few minutes of it.

Paul, it's BBCO0000002, and the clip we want is from 39 minutes and 20 seconds into the programme.

(Pause)

I'm sorry, I've given you the wrong reference.

Completely my fault, Paul, sorry. There was an update a year later of this programme and I've given you the reference to that.

It's BBCO0000004. Then from 39 minutes and 20 seconds into that programme.

(Documentary, Killer in the Village, played)

So that, as I say, was broadcast on the BBC, I don't know whether it was BBC1 or BBC2, on 25 April 1983.

That is probably the right point at which to stop for the day.

SIR BRIAN LANGSTAFF: Not bad timing. So thank you for that and we continue tomorrow. So we start at ten o'clock, do we?

MS RICHARDS: Yes. We'll finish this presentation on knowledge of risk and then turn to look at certain materials relevant to Professor Bloom and the Cardiff Haemophilia Centre.

There is a very long detailed note in relation to that which has been shared with core participants and their legal representatives and I won't be going through the detail of it. It will be a question of looking at some of the particularly key decisions and actions of Professor Bloom and the potential implications of those decisions and actions.

SIR BRIAN LANGSTAFF: Yes, thank you very much.

Until tomorrow then, and stay safe.

(4.33 pm)

(Adjourned until 10.00 am the following day)

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