Friday, 25 June 2021

(10.00 am)

(Proceedings delayed)

(10.05 am)

Presentation by Counsel to the Inquiry re Lord Mayor Treloar School and College (continued)

MS RICHARDS: Sir, before I come to some documentation relating to research undertaken at Treloar's, there are a handful of further materials and observations from the evidence about issues relevant to treatment, communication with pupils and parents, and issues of consent.

One document we haven't looked at yet is a book written by Dr Aronstam called Haemophilic Bleeding.

Soumik, it's RLIT0000666. We can see it's called:

"Haemophilic Bleeding; Early Management at Home."

If we go on I think about six pages, Soumik. Sorry, the page before that, I think. Yeah.

We can see the date of publication, so it was published in 1985. I'm not entirely sure, sir, when precisely in 1985, or when precisely written, but clearly written by then.

If we could go then just to the preface. It's

about another five pages on, please. That's it.

I just wanted to read what Dr Aronstam says in part here and then look at one particular passage in the main part of the book. He says:

"One hundred and fifty severely affected adolescent haemophiliacs have passed through the Lord Mayor Treloar College since 1973. They have been treated for bleeds at the Treloar Haemophilia Centre more than 15,000 times. Information on all bleeds has been recorded and many lessons have been learned. Mistakes were made, failures have been analysed and management regimes have been altered. This book is really the book of those haemophilic boys, for it is a distillate of the experience gained from the observation and treatment of all those bleeds over all those years.

"My own personal involvement began in 1977 when I was suddenly faced with the responsibility for the clinical care of 55 severe haemophiliacs boarding at the College, far from their homes and from the expertise of their own Haemophilia Centres. An immediate treatment strategy had to be devised and this was based initially on the results of an analysis of the crude data available from 5,500 bleeds which were seen and treated at the College between 1973 and

1977.

"From then on we began to collect data in depth on each bleeding episode. Constant review and analysis of these data have enabled us continually to update our practice and many of our innovations have been confirmed by controlled clinical studies.

"The information and recommendations in this book represent the Treloar Haemophilia Centre view of current best practice -- within a residential institution. I believe that extrapolation to everyday living is a valid one but recognise that the practicalities of our approach are not always appropriate. This reservation is stressed repeatedly in the text. I should also point out, however, that best treatment is best treatment however inconvenient. Our experience and our recommendations are on offer. It is for the haemophiliac or his adviser to balance the severity of his bleed against the urgency of his commitments and his assessment of the long term consequences of possible under-treatment."

Those are just some introductory observations that Dr Aronstam made. The particular passage I wanted to go to is in the chapter on prophylaxis. If we just pick it up at page 106, please. We can see there the heading "Prophylaxis", then Dr Aronstam

talks about "Long-term prophylaxis", and says in the second paragraph:

"Some haemophilia doctors put young children on long-term prophylaxis in order to prevent haemophilic arthropathy. Rather higher doses and frequency may be needed since any joint bleed can initiate the process."

Then he talks about "Limited prophylaxis":

"... prophylaxis given for a fixed period of time, usually from one to eight weeks. Limited prophylaxis may be given for target joints ... It can also be prescribed for periods of stress such as examinations when bleeding may be more frequent in certain individuals. A 'bad patch' which many haemophiliacs undergo periodically can be another indication for limited prophylaxis".

Then if we go over the page he then talks about "Single dose prophylaxis":

"This is the giving of one dose of factor VIII to cover a 'one-off' situation. This may be a high-risk event such as a sporting occasion. Such an event may be high risk even when the haemophiliac is not playing. A major event such as the Cup Final could involve a long and heavy journey a lot of jostling, a large crowd and a lot of excitement.

I would always advocate a dose before such an event. There are also occasions which are not in themselves high risk but are of such social significance that a bleed would be disastrous. Weddings and examinations are obvious instances. I am quite liberal in this matter and extend my list to include discotheques, important dates and Christmas shopping. My philosophy on the whole is that if it is important to a patient it warrants a prophylactic dose. I let him decide."

Of course, whether that is an accurate characterisation of the actual approach to treatment at Treloar's will be a matter ultimately for you to decide, sir.

SIR BRIAN LANGSTAFF: Well, it doesn't entirely fit with some of the evidence we've heard this week about those who didn't want to have it.

MS RICHARDS: Yes. Well, it doesn't fit in terms of the evidence in relation to prophylaxis. Perhaps more generally, it doesn't necessarily fit with any of the evidence we've heard about the provision of information in relation to the obtaining of informed consent.

"This category at our Centre gets the highest doses. Once we accept that a bleed must be avoided we

can't take choices. At least double our standard dose is indicated."

Then we have a paragraph, and the reason for going to this page, really, is because this is the only paragraph I can find in the book which refers to either hepatitis or AIDS. It's certainly the only page referenced in the index in relation to those subjects, and this is in 1985.

"No one could possibly argue that the infusion of a plasma product such as factor VIII for bleeding is unnecessary. The same can clearly not be said for prophylaxis. The risk of complications such as hepatitis and AIDS makes prophylaxis unacceptable to some doctors and some haemophiliacs. Extensive discussion on this subject is beyond the scope of this book. I feel very strongly, however, that this is a matter you should consider after discussion with your own doctors. Even if they feel prophylaxis is indicated, the ultimate decision is yours. It can, however, be very helpful to hear the objective views of someone who is not as emotionally involved as yourself."

That, as I say, is the only indexed reference to either AIDS or hepatitis, and certainly on a skim of the entire book I haven't identified any other

references to it.

SIR BRIAN LANGSTAFF: What this is indicating in 1985 presumably a lot of the text prepared either earlier in '85 or late 1984, is a collaborative participative approach to treatment.

MS RICHARDS: Yes, absolutely, and one of the issues for you to consider is whether the reality lived up to what Dr Aronstam is here describing as being a proper approach.

SIR BRIAN LANGSTAFF: He obviously is recognising, at least at an intellectual level, that, at least so far as other doctors are concerned and other patients are concerned, they should talk about it with the doctor and reach a joint decision and the decision is the patient's.

MS RICHARDS: Yes.

We can take that down, thank you.

Then looking broadly at the question of communication with patients, we've heard, both in 2019 and the oral evidence we heard then from witnesses who had attended Treloar's, and in the course of this week, evidence about what individual pupils were or were not told and what their parents were or were not told about risk at testing and so on.

In terms of hepatitis and information about

hepatitis, you'll recall the evidence of Nick Sainsbury talking about being told there were two types of hepatitis, the fatal kind and non-fatal kind, and you'll recall his evidence about remembering in relation to that outbreak in the mid-1970s the red mark on the plate to identify which boys have hepatitis. There is another witness, the sister of a pupil at Treloar's, who also recalls her brother's cutlery and crockery being marked because he was infected with hepatitis so that recollection is not unique to Nick.

Then if we look at WITN3224001, please.

This is a statement from another pupil at Treloar's. If we go to the second page we can look at paragraph 9 towards the bottom of the page.

"While I was at the LMT, I was informed that I was infected with Hepatitis B. I was still a minor at the time, and I do not recall my mother ever being told about this diagnosis. She certainly never told me she had. A group of pupils were told collectively that we had been tested positive. We were also told that because we were Haemophiliacs we would get over it unlike other people."

Sir, again, that may be, in broad terms, again consistent with the kind of recollection Nick

described, of essentially being told, "It's not something for you, as a haemophiliac, to worry about". And that's the broad sense that emerges from the evidence overall that the Inquiry has received.

In relation to communication about HTLV-III/HIV and AIDS, there's a range of evidence the Inquiry has received. Again, some we've heard orally in 2019 and this week. Others are in the form of written statements. One witness recalls a pupil, a roommate, not returning to school after half term. People were asking what had happened, and being told not to worry, that people would be looked after.

Some witnesses have recalled some kind of meeting with pupils at some stage regarding AIDS, in which they were told, "Don't worry, only two people in the UK with haemophilia have AIDS", so an attempt to provide reassurance. And another witness, a mother, recalls her sons being invited to a meeting at which they were told that there was information about AIDS and haemophiliacs in America but it was not something for the pupils to worry about.

In relation to how individual pupils were informed that they had tested positive for HTLV-III, the evidence that the Inquiry has received and heard suggests that there was not a single uniform approach

adopted. So, as you've heard, there are witnesses who recall being told in a group with other pupils, being told in a matter-of-fact way, or being told essentially, "You have it, you don't, you have it, you don't."

There are others who recall being told on their own by Dr Aronstam, possibly with others.

You've heard, and we had evidence this week, that there appears to have been the communication of that information over quite a long period of time, in the sense that there are some who, it appears, may have been told in 1985, but others who may not have been told until 1986. Which raises the question about there being delays, given that we know that Dr Aronstam certainly had a number of results by March of 1985, and yet evidence of possibly as much as a year or more before the individual is told.

And of course, we've heard evidence this week which suggests that some pupils may not have been told at all and you'll recall the extremely powerful evidence of John Peach in that regard about his sons.

And, of course, evidence which paints a picture that for the most part, parents do not appear to have been told directly by Treloar's, by the Haemophilia Centre, of their child's diagnosis.

I say for the most part. There is some limited evidence of parents recalling being told themselves but for the most part that's not the picture which emerges from the evidence.

We know from the evidence we heard yesterday that the headmaster was not involved in the process of pupils being given this information, or involved in the process of ensuring that parents were given that information and the evidence that we have from Mr Scott, the housemaster, or one of the housemasters, indicates that he was not involved in that process.

So that which the vast majority of pupils recall, in other words that they were told by the staff at the Haemophilia Centre, it seems to be consistent with all the evidence that we have. There doesn't appear to have been any consideration given to having someone there, whether parent or housemaster or someone else *in loco parentis*, to provide emotional and pastoral support at what must have been a horrific time.

The evidence, then, about what support was available to pupils given this information is at best equivocal. Again, you'll recall Mr Macpherson's evidence, his understanding that there was, in principle at least, a psychiatrist, and a counsellor

available, and there is evidence to suggest that that was a facility that was available across the school as a whole. So we have a statement from Ms Burton, who was the headmaster's secretary for a period of time, who recalls there being counsellors at the school, but not a structured or organised arrangement in relation to the haemophiliac students for them to be seen specifically.

And if we go to the statement of Mr Scott, the housemaster --

SIR BRIAN LANGSTAFF: Do we have any information as to when the counsellors began their work? Were they there for anyone at any time?

MS RICHARDS: So my reading of the evidence, sir, is that there was no specific counselling facility that was introduced into the school to address the HIV diagnosis and the position of haemophiliac patients being given this diagnosis and supporting them.

The evidence suggests that there was some form of broader counselling service that might have been available to all pupils as a matter of generality.

SIR BRIAN LANGSTAFF: Yes. Certainly the headmaster had a number of relatively scathing things to say about the way in which pupils were told, which he had not -- assuming that the evidence is accepted -- which he had

not understood.
MS RICHARDS: Yes.
SIR BRIAN LANGSTAFF: Before hearing it here.
MS RICHARDS: If we go to the statement of Mr Scott at WITN5314001.

Mr Scott was a housemaster at Treloar from 1981 until his retirement in 2011 and, if we go to page 8, he says in paragraph 41:

"In general terms I would consider the training which I received to have been 'fit for purpose' in its time, but with the benefit of hindsight, I feel that it was perhaps lacking as regards supporting those with HIV and/or AIDS."

The next paragraph:

"Clinical staff from the Treloar Haemophilia Centre attended to explain medical information as regards HIV/AIDS to staff, such issues as its means of transmission, safe disposal of clinical waste and in particular care that had to be taken around blood, so we did receive some useful instruction, but there was a lack of training which would have enabled staff to offer psychological support to infected students."

Sorry, and the next paragraph:

"This particular requirement was beyond anything which my past experience and training had prepared me

for, and I found myself ill equipped to address individual concerns when they were suddenly presented with an HIV diagnosis and confronted with questions as to what HIV/AIDS could mean for them."

So that was Mr Scott's recollection.

Then if we can go back to a document we've looked at a couple of times before, it's Dr Aronstam's 1986 report to the region.

It's at HHFT0001073. So it gives us some information about counselling and other matters.

If I pick it up at the beginning:

"The steady evolution of this Centre has been shattered by the impact of AIDS HIV infection which will exert a major influence on our policies for several years to come. We have had to reassess our priorities and this report will consider only those of major relevance. The consumption of Factor VIII is still clearly important and our patient population and therapeutic policies are significant influences on this. AIDS/HIV has added considerably to our workload and there are other financial implications related to therapy."

Then he refers to the Centre extending its expertise from bleeding into offering a broader service in relation to clotting.

Then if we go down the page, I referred yesterday to the second paragraph under the heading "AIDS/HIV", which referred to there being 43 patients antibody positive.

If we go to the next paragraph, he says:

"Many of our patients are now showing clinical evidence of HIV disease."

And further details are given in that regard.

Towards the bottom of that paragraph he says:

"We are likely therefore to have seven further cases of AIDS within the next year or two and I predict twenty to twenty-five cases in my haemophiliac patients by 1990. There are gloomier predictions about which suggest that up to 100% of the infected haemophiliac population will eventually succumb to the virus."

Again, sir, you may wish to contrast what Dr Aronstam was saying there with what we've seen referred to from time to time elsewhere about saying, at least saying at some stages to others, we don't know how many people will progress to AIDS, probably a very small proportion of people will progress to AIDS. At least by 1986 it appears that is no longer Dr Aronstam's view.

Then he continues:

"The bare facts do not reveal the cataclysmic impact of the AIDS/HIV problem on our Haemophilia Centre. The patients, their families, the Haemophilia Centre staff and the community around us are all profoundly affected and will continue to be so for many years to come. We at the Centre have had to devise a multi-faceted strategy for responding to many different situations [if we go to the third page, please, Soumik] which have arisen and others which will arise in the future. Naturally, there are implications for resources."

Then we see a heading "Counselling", in which Dr Aronstam says this:

"All haemophiliac families, affected or not, are encountering prejudice. They need support to deal with this and the community around needs education.

"Adult haemophiliacs with the antibody live a life haunted by fear. They need constant support, and follow-up visits, which are now much more frequent, require much more time at each visit. Parents of children with HIV are devastated and need even more support and time. They are plagued by prejudice at school and in the neighbourhood and the solution is to go out and educate but this requires time.

"Antibody positive haemophiliac children enter adolescence with an increasing viral load. Nature has programmed them for sexual experimentation at a time of maximal infectiousness. The counselling involved in this situation must be expert, intense, patient and even more time consuming if breakout of the virus from this group is to be averted.

"The advent of full-blown AIDS demands support for the dying and for those who will be bereaved. It is also important to realise that the advent of AIDS is not just a matter of coming into hospital and dying. It takes three to four years to die and in between hospital admissions there are long periods when the sufferer is at home, becoming weaker and increasingly a drain on community resources. It is during these times that the Haemophilia Centre must remained involved. We cannot be seen to abandon those who we have accepted as our lifelong responsibility."

Then he poses the question: "Who should counsel?" And this may give us some insight into the availability of counselling at the school. He says:

"In our Centre I and a nursing sister have done it all up to now."

So there is no suggestion there of additional counselling or extent of counselling available.

"The specialised nature of the haemophiliac condition makes it impossible to win the trust of the patient unless you are seen to have a thorough understanding of the primary illness. For this reason I do not see a role for the injection of specialised counsellors into our Unit. We have been allotted a social worker from the local Department of Social Work who will spend one morning a week at the Centre. She will naturally be involved in social work with our patients and I hope will be able to take on some of the counselling load but obviously only a minor component. I see myself as continuing to play the major role in this area with the nursing sister. She is young and in the nature of things likely to move on in the next year or two. Continuity with the haemophiliac families must be preserved."

Then there's a reference to the need for ongoing medical surveillance, for immunological surveillance, where he says:

"I believe it is essential to monitor the T-cell markers, and we have had to develop the technique in our own laboratories because of logistical difficulties in getting fresh samples to Southampton. This work is done by Haemophilia Centre staff."

Then there's a reference to treatment and the

possibly of AZT.

That's the report that Dr Aronstam made to the Wessex Region, the Regional Health Authority in, as I say, we think 1986.

SIR BRIAN LANGSTAFF: Was any part of this report asking for finance for a counsellor?

MS RICHARDS: No, it's a request for continued funding, certainly. That, I think, is the purpose of it.

If we go to page 7 -- actually, I should have referred to this. This provides some further information about Dr Aronstam's involvement. He says:

"I am contracted to do five sessions a week (mornings) at the Haemophilia Centre and five sessions a week (afternoons) at the Department of Haematology, Basingstoke District Hospital."

Then he refers to the difficulty of what he says is maintaining his commitments to the Haemophilia Centre, and he lists, amongst other things, the increased counselling commitment as well as increase in administration and paperwork consequent upon the HIV situation, and he refers to his involvement in various groups and working parties.

Point 7, he describes himself as a trained AIDS/HIV counsellor. He says:

"... I have many patients referred to me for

counselling who are not haemophiliacs."

He says in paragraph 8:

"I view the above as obligatory commitments. There are, however, other commitments which it would be irresponsible to ignore. Our experience at Treloar's is almost unique and it is essential that it is documented. Coordinating the necessary collection of data and communicating the information must be done and is time consuming."

Then he is essentially making out a case for a further full time consultant, in what follows.

If we go to the next page he talks about predictions and future requirements in relation to funding. So he's asking for increased funding for the laboratory, pay increases for staff, a third consultant, funding to enable Centre staff to visit patients in their home, funding for attendance at education and conferences.

SIR BRIAN LANGSTAFF: Now, I think you're on a page which is not on the screen.

MS RICHARDS: I'm so sorry, that's entirely my fault. It's the page after that. I should have looked at the screen. So you'll see here, sir, heading:

"Predictions and future requirements."

He is setting out here what he thinks the future

requirements of the Centre are and what will need enhanced funding, so he refers to "The Laboratory" and then the heading "Medical Staff", underlined, in relation to pay increases for medical staff. He refers to the need to appoint a third consultant haematologist, funding to enable Centre staff to visit patients in their home, and then under the heading "Education/Conferences", funding to enable staff to keep abreast of current developments nationally and internationally.

If we go over the page, what else is listed there are all examples of the kind of conferences and meetings he thinks staff should be funded to attend. And then there's some reference in terms of spending and revenue. So, no, there's no financial case there put for the appointment of a counsellor to the Centre.

SIR BRIAN LANGSTAFF: No, but the -- I suppose the context in which he is saying "I do all the counselling" is saying that: AIDS is taking up a lot of his time. It inevitably imposes demands. Those demands are real. Please, therefore, appoint somebody else to share the load.

MS RICHARDS: Yes, absolutely.

SIR BRIAN LANGSTAFF: Not the load of counselling but the load of --

MS RICHARDS: Of the general haematology work.

SIR BRIAN LANGSTAFF: -- allowing me to do what I have to do to fulfil my obligations to those who are my patients who have suffered from HIV infection.

So there is a motive for his --

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: -- for up-playing his own role and downplaying the role of others, but it still doesn't entirely explain, unless he is simply not mentioning it deliberately, the absence of any reference to counselling being available through the school.

MS RICHARDS: Yes, you're right. It doesn't mention it at all and I don't think there's any evidence to suggest that there was any kind of specialist counselling available through the school in any event. And you've seen what Mr Scott had to say. But you're right, it doesn't refer to that.

SIR BRIAN LANGSTAFF: One way or the other I have to make sense of what the headmaster told me yesterday as against this contemporaneous account, albeit with a motive, and Mr Scott's account.

MS RICHARDS: Yes.

And then in terms of information being provided more broadly to parents of pupils at the school as opposed to information about children's diagnosis

being provided to individual parents, Mr Macpherson referred, I think, to a letter sent out by Dr Tomlinson to try to reassure the parent cohort as a whole about the risks of AIDS.

It may be he was referring to the document at RLIT0000663.

Certainly the minutes of governing body meetings that we have do refer to Dr Tomlinson writing to parents.

This is a letter -- the date is not clear in the top right-hand corner, as you'll see, and zooming in doesn't help either, unfortunately. It's on 19 September 1980-something, but that's the best I've been able to do. But it says:

"Dear Parents,

"You will no doubt have been concerned, as we have, by the treatment of a haemophiliac boy in a Hampshire school and the interest in this that has been aroused by the media."

You'll recall Mr Macpherson not having any particular recollection about media problems.

"As you know, we've always had haemophiliac boys at this school, so that they have been able to have immediate treatment and also continue their education. They have always integrated well with the children

with other handicaps.

"We have been aware that the treatment the haemophiliacs have had has now led to the risk of infection with the virus which causes AIDS and we have taken this very seriously. We have watched the results of all the research being done, and have been in touch with all the leading specialists in this field. We are being extremely cautious and are assuming that any haemophiliac boy could be a carrier of the virus. Even if this is so, the chance of any of them eventually developing AIDS is very small."

And there is a contrast with what Dr Aronstam was saying in his report to the region.

"The infection is extremely difficult to spread, as the virus dies immediately it is outside the body.

"We are confident that the precautions we take at the College make it impossible for the virus to be passed on to any child or member of staff at the school. The only risk we are left with is that of close and intimate sexual contact with a possible carrier of the virus, and this is of course against the College rules and we trust the pupils will not put themselves at risk in this way.

"We will continue to take every care, and we assure you that the safety of the other children and

the school staff is our first concern. We also have a responsibility to ensure that the haemophiliac boys should be treated in a humane way and not unjustifiably ostracised.

"If you want any further information about this, or details of the precautions being taken, please do not hesitate to contact me or the Headmaster either by telephone or by arranging to come and see us."

We can see the letter is from Dr Tomlinson, the school medical officer. So that appears, on the face of it, was a letter seemingly designed to reassure the parents of all the pupils at the school that they should not be concerned about HIV being passed on amongst pupils at the school.

SIR BRIAN LANGSTAFF: Just as you've been talking, my mind is still thinking about the counselling question. Does any -- do any of the statements we have from those who were actual pupils, or those who are the parents of or family of those who were pupils who are no longer with us, say anything about them being -- having any form of counselling which might meet the description?

MS RICHARDS: I don't think so. There are entries in medical records in the correspondence that refer to the nursing sister, Jane Kershaw, the nursing sister

at the Centre, having conversations with one particular pupil about diagnosis and its implications.

In terms of any form of specialist counselling or counselling other than through Dr Aronstam and the nursing staff at the Centre, I can't recall anything.

I'm going to see if Ms Fraser Butlin has any recollection -- no, hers is the same as mine -- from the statements we've read, and I think we've read all the statements the Inquiry has received which describe attendance at Treloar's, either directly from a pupil or from a family member. We've not detected anything which refers to any form of external counselling within the school or elsewhere.

SIR BRIAN LANGSTAFF: Yes, thank you.

MS RICHARDS: Just to get a sense of what the nursing sister was talking about, if we go to TREL0000222_033.

This is a letter -- this is a number of years on now in the Centre, September 1989, but it's a letter from Jane Kershaw at the Haemophilia Centre to a nursing sister at the Oxford Haemophilia Centre and it's about a couple of specific pupils who have recently left Lord Mayor Treloar College and will be reverting to the care of the Oxford Haemophilia Centre.

It refers to Dr Wassef writing to Dr Matthews

about the clinical aspects of their care, and then what you might regard as counselling aspects are then touched on in Jane Kershaw's letter.

So she says in paragraph 4, in relation to one of the boys that:

"[He] is fully aware of his status and all its implications, many discussions have taken place on the subject of HIV and AIDS and also regarding relationships and related emotional issues."

She refers to him harbouring "quite a lot of anger about the situation aggravated by some negative experiences". She also refers to having had some contact with the parents of one of the boys and, in relation to the other boy that she's discussing, there is a discussion about whether that individual should be told his HIV diagnosis.

So it's apparent from what is set out in this letter and over the page -- and I'm not going to go to it because there is quite a lot of detail about the individual family even though it's redacted, so we won't go to it, thanks, Soumik. We'll just go back to the first page.

But there's a discussion which makes clear that there's one particular pupil who hasn't been told their HIV diagnosis, albeit it is described as being

at the request of the parents.

So that's -- we've referred to that because it's a relatively -- it's one of relatively few pieces of documentation which show those kind of discussions, the kind of discussions that you might think counselling would encompass taking place, but it's with the nursing sister and, as we see, it's rather later on in the course of the 1980s rather than at that particular point in time when boys were being told their diagnoses and might have needed maximum support.

SIR BRIAN LANGSTAFF: Yes, thank you very much.

MS RICHARDS: Then just a couple of further documents.

If we go to TREL0000365.

These are the extracts from minutes of a governing body in February 1986.

Sir, you asked yesterday if we knew when the first reference to AIDS was in the governing body minutes, and the answer is we don't appear to have all the governing body minutes so we're still checking to try and find out what the position is in that regard.

But if we go to the second page, I looked at one paragraph from this with Mr Macpherson yesterday but if we perhaps just look at the rest of the discussion under the heading "AIDS":

"The Headmaster commented that the correct inference to draw from the Minute on this subject from the last Meeting was that although 'very few' of the haemophiliac boys carrying the AIDS antibodies would develop AIDS, this meant that at least one would do so at some stage."

So, again, there appears to be something rather different being said here to what we see in Dr Aronstam's report to the region, which is a much bleaker and, one might think, more realistic assessment of the situation.

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: Then there's a reference to advice from Dr Aronstam about the risks of transmission, so:

"... a pupil actually suffering from AIDS posed no greater danger to the other pupils and staff in the College than any of the pupils carrying the AIDS antibodies."

The advice being that it's the person with AIDS who might in fact be at risk of being infected by others with opportunistic infections and the like.

SIR BRIAN LANGSTAFF: So certainly at this stage he wasn't taking the view that the AIDS antibody might be protective?

MS RICHARDS: No. No, that's right.

Then we can see at what's said to be a meeting that had taken place between the headmaster and senior staff to consider the action that should be taken once it was determined a pupil was actually suffering from AIDS, as opposed to merely carrying the antibodies. And there's reference to a three-stage process:

"Stage 1: When a pupil had been identified as actually suffering from AIDS, he would not be asked to leave the College. Information on his condition should be restricted to the parents and Headmaster, and to Nurses and Senior staff who needed to know."

Again, that's not necessarily consistent with what to we saw yesterday about the school staff or the headmaster not actually knowing which individuals were infected, but in any event.

Stage 2 is described as:

"When a pupil is suffering from an 'opportunistic illness' exacerbated by AIDS he will be nursed in the College Sick Bay, provided he is not too severely ill."

Stage 3 was:

"When the pupil becomes so weak as to be unable to benefit from further teaching (but not before) he/she would be transferred to their home or hospital for permanent nursing care."

So that's -- well, perhaps if we just look at the bottom of the page. I think I referred Mr Macpherson to the suggestion that the parents of pupils were aware of their son's infection. Obviously there's evidence to the contrary.

But then we can see a reference to the public relations problems that might occur, and if we go to the top of the next page, we see identified in the second paragraph a further reference to public relations. So we see Dr Whitfield emphasising his view that "the College's policy and procedure" was "exemplary", but suggesting:

"... it might be advisable to make contact with the ... Health Authority for advice on how to handle the public relations aspects of these matters."

The evidence in relation to pupils being told about their hepatitis C diagnoses that the Inquiry has received is much more limited, possibly because a lot of those who have given statements to the Inquiry received their diagnoses after they left Treloar's and were receiving their diagnoses from their home Haemophilia Centre. So the information is rather more limited.

We've got a statement where a witness recalls being informed by Dr Wassef about infection with

hepatitis C, and his recollection that he was told it would kill him but Dr Wassef wasn't sure how long that process would take. So essentially told it was something serious.

Another witness recalls their parents being told at a meeting in Treloar's of the infection with hepatitis C, but the gist of that was, "Well, your son will be fine", and just to get on with life.

Again, another recalls just being told of hepatitis C but not really being given any further information at all.

There's one set of documents which does provide an indication of a delay in a patient being told their diagnosis. So we've got a test result from mid-1990 and evidence which suggests that the test result was communicated in around mid-1991, so a delay there of a year.

Then just a couple of documents more broadly on treatment for hepatitis C.

If we go to TREL0000313_066.

This is a letter of 12 July 1991. I may have referred to it yesterday, I'm not sure, in the context of -- if we look further down the page -- in the last paragraph there's a discussion there about non-A, non-B hepatitis. So we can see there's a reference to

a liver examination and Dr Wassef says:

"I explained to him that he has antibodies to HCV (non-A, non-B) ..."

I'm not sure why in July 1991 the term "non-A, non-B" was being used rather than hepatitis C but in any event the letter continues:

"... and that almost all haemophiliacs got that through Factor VIII transfusions in the past. I have explained the significance of this and the possible long term effect."

And Dr Wassef describes passing that information on to the pupil's mother and providing a copy of a Haemophilia Society Bulletin article.

Then at the bottom of the page Dr Wassef says:

"We will be seeking advice regarding management of this condition following the recent publications on the value of Interferon in some cases of HCV infection."

So a tentative reference there to the possibility of treatment with interferon.

Then if we go to TREL0000137_046.

This is a letter from 20 November 1995. It's from Dr Wassef to a Professor Arthur at Southampton General Hospital. It's not specifically in relation to a Treloar's pupil. It's in relation to a catchment

area pupil. But, again, it provides some indication of the broader picture in terms of availability of treatment:

"Although I am aware of the ongoing dialogue between yourself and Dr Aronstam regarding arrangements to see all our Haemophilia patients with antibodies to HCV sometime in the near future, this is a 'one-off' patient whom I would be most grateful if you would kind enough to send an appointment direct to see you as soon as you possibly can."

Then there are details given about the specific patient, and their concern about consequences of hepatitis C.

So it tends to suggest that, in terms of referral for treatment and advice for the hepatitis and the liver care more generally, as at November 1995, that was still a matter in discussion as between Dr Aronstam and Southampton General Hospital, rather than there being by that point in time any specific arrangements to seek expert hepatology or care from a consultant physician (inaudible).

If I then just deal with an issue which has recurred throughout the oral evidence this week, and that's the question of consent or informed consent to

treatment and to testing. You obviously have heard the oral evidence both from 2019 and from this week, and we've referred in our written note to a number of other witness statements and documents in this regard, drawn from records, correspondence, and so on from the Treloar's material. It'll obviously be a matter for submissions in due course and for your judgment in due course, sir, but the evidence certainly that we have seen to date would tend to suggest, not by a slim margin but overwhelmingly, that parents were not told, or at least there was no system or process in general operation for telling parents of risks of viral infection, and the same true in relation to pupils.

Parents were not given details about or even core information about their children's treatment at Treloar's for haemophilia, and you'll recall again the evidence of Mr Peach, not aware that his sons were being switched from receipt of the NHS Lister concentrate to multiple American concentrates and there are similar examples in the material that we've referred to. Parents not being told that AIDS-related investigations or tests were being undertaken, or that pupils were being monitored for the stigmata of AIDS and, likewise, pupils not being told that.

And then, in relation to hepatitis, and with the

exception of some evidence of parents being given information in that 1974/75 outbreak, the evidence suggests parents were not systematically told if their sons were believed to have been infected with hepatitis.

There is no particular evidence to suggest, again, any systematic approach to informing parents about non-A, non-B hepatitis or the significance of abnormal liver function tests. Pupils appear to have been given limited information of the kind described. They might have been aware of friends going yellow, but hepatitis essentially portrayed as something that was not something that they needed to be concerned about.

Then, again, the evidence that we've seen tends to suggest that neither pupils nor parents were told that children were being tested for HTLV-III and, not having been told, were obviously not in a position to consent to that process of testing. Then of course, the evidence suggesting that parents for the most part were not told the outcomes of those tests.

Certainly, we've looked in the course of the week at some examples of medical records, and we've looked at where there have been in 1983 examinations being undertaken for immune system disturbance,

looking at lymph nodes, weight loss, etc, etc. So we've seen examples of those kinds of examinations being recorded in the notes. We've seen multiple examples of letters being written to the home clinician both in 1985 -- sorry, '83, '84, '85.

What we have not seen are any records which record the communication of the diagnosis to the patient. So we do not see for those witnesses whose records we've looked at, either for the purposes of their oral evidence or for the purpose of examining the material more broadly, entries which say, "Saw X today, informed X of their HTLV-III test result, counselled X about their HTLV-III test result."

That kind of information simply does not appear to have been recorded, at least in any of the records that we have.

In terms of the impact of everything that I've referred to, everything that we've heard in the course of the week upon pupils, I'm not going to try to summarise the powerful, emotional, eloquent evidence that you've heard because I would not do it justice. But everything that you have heard, sir, and read, paints a very clear and powerful picture of the effect that this has had on individuals' lives and, as I say, I would do it an injustice if I tried to summarise it.

Sir, before then I turn to the question of research, there's one short video clip to play, which is just -- it's a brief interview of a kind with Dr Aronstam.

So if we could play that, please, Soumik.

(Video of Interview with Dr Aronstam played)

SIR BRIAN LANGSTAFF: The date of that?

MS RICHARDS: We'll check. I don't know off the top of my head. It's obviously presumably around the time of the first --

SIR BRIAN LANGSTAFF: Oh, the setting up of the Macfarlane Trust?

MS RICHARDS: Yes, exactly.

SIR BRIAN LANGSTAFF: So it would have been sometime in 1988, probably.

MS RICHARDS: Probably. It's late eighties, I would have thought.

SIR BRIAN LANGSTAFF: Yes, or late '87. But it was the end of '87 it was announced, Macfarlane and, given the content, it sounds like before the first of the Macfarlane special trusts.

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: Special payments.

MS RICHARDS: Yes. We'll check. It's on, I think, the Tainted Blood website, that video, so I'll see if

I can find out what the date was.

Sir, I'm then going to come to the question of research. I use that as a very general heading. What we'll see is there are references to research, to trials, to studies, on multiple occasions in the documents. It is not always easy to piece together, for example, if one has something that looks like a consent form or an entry in records referring to a trial, what trial or study or piece of research, is being referred to. But what is clear and what clearly emerges from the documentation is that research was regarded as a fundamental part of the work that was undertaken in relation to Treloar's pupils, really from the end of the 1960s onwards, and throughout the 1970s and 1980s.

I'm going to refer to a number of documents which show pieces of research being undertaken, but it won't necessarily be a comprehensive whole, because, as I say, it's not always easy to work out whether a document is referring to one particular trial or several trials, and if so, which ones.

SIR BRIAN LANGSTAFF: Do we have an idea of the total number of studies that might have been done, or the range within which that might have fallen?

MS RICHARDS: We don't, really. I'm going to be referring

to a number of studies and references to a number of projects, but it was an ongoing feature, if I can put it that way, so they are studies that many of them went on for a number of years. So whilst I can't give a figure to the number of research products or studies, what one can I think say is that there was always research being undertaken. If you take any one particular year, or even any one term, the picture that emerges is that there were studies, trials, or research, sometimes prospective, sometimes retrospective, being undertaken.

SIR BRIAN LANGSTAFF: I mean, Dr Rainsford was specifically appointed as a research fellow, was he not?

MS RICHARDS: He was, yes.

SIR BRIAN LANGSTAFF: And Dr Kirk was also, I think, a researcher?

MS RICHARDS: He was, yes. That was the basis for the appointment of each of them, yes.

But Dr Arblaster and Dr Aronstam, although appointed to undertake clinical roles, also very closely involved, particularly Dr Aronstam, with research undertaken at the college.

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: So if we just look at a handful of general

documents before the break, just to give a flavour of the role of research at the school.

If we go to AMRE000011_006.

SIR BRIAN LANGSTAFF: Now you're missing a --

MS RICHARDS: Oh, am I? Sorry. Five zeros. AMRE0000011_006.

SIR BRIAN LANGSTAFF: That's it.

MS RICHARDS: Sir, this is an undated document but it's from, I think, probably the first half of the 1970s because it's about obtaining funding for the appointment of Dr Kirk. But it also gives some background, some history in terms of the history of research at the college, and also a flavour of the importance of research.

So we can see the heading:

"Introduction

"Lord Mayor Treloar College is [a] unique establishment since there are more than fifty boys suffering from various coagulation defects (namely Haemophilia, Christmas Diseases and von Willebrand's Disease) in residence at the College for approximately 264 days each year. These boys usually come to the College at the age of eleven and leave at the age of sixteen to eighteen years of age. They are, therefore, under continuous medical supervision for

nine months of each year and often for many years.

"Day to day treatments afforded to these boys by the Treloar Haemophilia Centre which is under the direction of Dr PC Arblaster, Consultant Physician. This Centre was established three years ago and is now one of the best staffed and equipped Centres in the country. There are adequate laboratory facilities specialising in coagulation, under the direction of Dr A Aronstam, Consultant Haematologist, who is also Associate Director of the Centre. The boys are kept under orthopaedic supervision by Mr Francis J Moynihan, Consultant Orthopaedic Surgeon. The staff at the Centre consists of a Medical Officer, who is employed as full-time SHO in Haemophilia, a Medical Officer of consultant status, who is employed for [seven elevenths] of his time at the Haemophilia Treatment Centre and [four elevenths] as Medical Officer to Lord Mayor Treloar College and Florence Treloar School. These medical officers have the assistance of a team of Sisters and Nursing Staff."

Then we get to research.

"Since 1968, a Research Fellowship in Haemophilia has been established at the College by the National Fund for Research into Crippling Diseases. The present Research Fellow (with secretarial help --

also provided by the National Fund for Research into Crippling Diseases) has set up an organisation at the College and meticulous medical records are maintained."

That's a reference I think to Dr Rainsford.

If we go over the page, it continues:

"Lord Mayor Treloar College has a large, modern Sick Quarters built in [1958], which provides fourteen beds for in-patient treatment. It is fully equipped with a modern surgery, a physiotherapy department and consulting rooms and is staffed by three State Registered Nurses and two Medical Orderlies, all of whom have been fully trained, by the present Research Fellow Dr Rainsford, in the management and treatment of haemophilia."

Then there's a reference to a physiotherapist and the availability of hydrotherapy.

"Arrangements are such that any emergency can now be dealt with at the College. The present Research Fellow accomplished a great deal during his stay at the college, and was responsible in part for the research on which the foundation of the Alton Centre was based. It is anticipated that Dr Rainsford will stay in the locality of the School and continue to work part-time at the Centre for the next two to

three years, and be paid by the Regional Health Authority. During this extension of his work Dr Rainsford will support the Centre, complete his present research projects, and give assistance to the new Research Fellow."

"The present arrangements at the College are particularly suitable for a specific type of research into haemophilia and other coagulation disorders, namely the study of the relationship between laboratory findings and close day-to-day clinical observations. It is the only establishment in the United Kingdom which can provide the opportunity and the facilities for extensive clinical trials of various kinds of treatment which cannot, at present, be conducted anywhere else."

"A work of explanation is required about the proposed association of the new Research Fellow and Project with the Oxford Haemophilia Centre. There has been close liaison between the Oxford Haemophilia Centre and the care of haemophilic boys at the Treloar College for the last ten years and more. In the last year this type of association has been given recognition by the DHSS by a plan to organise Haemophilia Treatment and Research on a supra regional basis. It is proposed that certain supra regional

centres, of which Oxford Centre is one, shall be responsible for administrative duties such as ensuring an adequate supply of Factor VIII, providing a reference laboratory and teaching facilities, providing holiday support, determining the number of haemophiliac patients in their area of care and organising research on a regional basis. Alton is included in the region provisionally assigned to Oxford. In this new organisational framework it's hoped that exchange of NHS staff may be arranged between the Oxford Centre and that at Alton and it is proposed that the research facilities of the Oxford Centre should be available to the Research Fellow at the Treloar College. It is our opinion that the basic NHS organisation at the Treloar College is now such that a young Research Fellow could work for and obtain a research degree by working both at the College and at Oxford. The present application is for financial support of such a fellow."

Then we see the heading:

"The Research Project."

"The Research Project is entitled 'The Promotion of Haemostasis in Patients Suffering from Congenital Deficiency of Blood Clotting Factor VIII or IX'. The research will form the basis of a research degree to

be submitted by the fellow to a [UK] University.

"Clinical and pathological observations made during the last six years at Lord Mayor Treloar College, on boys suffering from haemophilia, strongly suggests that frequency and duration of spontaneous bleeding is not solely due to a deficiency of the known coagulation factors ... The most important fundamental discovery concerning the diathesis of haemophilia made over the past few years is probably the recognition of Factor VIII related antigen. At present the nature and function of this factor remains to be determined. Investigations ..."

Sorry, this bit is rather faint -- and then there's discussion about investigations on von Willebrand's.

I'm not going to read all of this out but it refers again to findings at Treloar College already published in a 1971 publication.

"It is suggested, therefore, that we should concentrate on this aspect of research in the near future."

Then if we go to the next paragraph down it says this:

"The existence of commercial concentrates of human Factor VIII has led to much more liberal use of

fractions prepared from large donor pools in the treatment of haemophilia. The consequences for the patients of this increased treatment are improved protection from crippling deformity and much extended horizons of possible activities. But the danger of contracting the blood-borne viruses causing hepatitis is also increased. The residence of these boys in one place provides an ideal opportunity to study this complication of treatment.

"The Project will have two main aspects:

"1. Laboratory.

"2. Clinical planning and observation."

Then if we go to the next page, there's a discussion under the heading "Laboratory Observations". It says:

"In the laboratory observations will be made on the levels of various important plasma constituents in relationship to the clinical state of the boys at the Treloar College and to observe the effects of treatment on these constituents."

Then there are various particular aspects of laboratory observation that are then recorded.

If we go just over halfway down the page we'll see that paragraph (d) refers to:

"Liver function tests ... SGOT, SGPT [et cetera]

will be carried out at regular intervals on blood samples which are collected at the time of infusions given to the boys. These samples will also be tested for [I think that's probably hepatitis B antigen and antibody]. An attempt will be made to trace the source of infection in every instance of [the patients] however mild clinically. Some of the tests proposed may give abnormal results in response to conditions other than viral hepatitis and such associations will be recorded."

"(e) Observations will be made on blood samples from boys having antibodies to Factor VIII in an attempt to determine the natural history of such antibodies in the patients."

Those are some of the laboratory studies proposed. Then in terms of "Clinical Studies":

"Depending on the results of the current trial of prophylactic therapy being completed by Dr Rainsford [and I'll come on to the prophylaxis studies] there may well be the need to hold a new prophylactic trial [then this bit is very faint] with increased ..."

Sorry, can we just look at the very first --

SIR BRIAN LANGSTAFF: "... increased and more frequent dosage of Factor VIII."

MS RICHARDS: Thank you, sir.
SIR BRIAN LANGSTAFF: I think it is probably better actually not highlighted.
MS RICHARDS: I think it probably is, yes.
SIR BRIAN LANGSTAFF: Because it's easier to read, I'm afraid, in the original.
MS RICHARDS: Then it refers in the next paragraph to:
"The careful studies of the records already carried out by Rainsford and ..."
I'm not sure who the second name is but it's reference to a publication --
SIR BRIAN LANGSTAFF: "Hall" it looks like, but it's difficult.
MS RICHARDS: It looks like. Then there's a reference to a publication in the British Journal of Haematology:
"... will form the basis for comparison in all clinical studies. These records will be [something] to ensure compatibility with previous observations and to provide the background against which to [something]" --
SIR BRIAN LANGSTAFF: "Provide."
"... provide the background against which to [ensure] the effects of treatment."
MS RICHARDS: Yes, "to ensure" --
SIR BRIAN LANGSTAFF: "... to measure the" --

MS RICHARDS: "To measure", thank you, sir.
"... to measure the effects of treatment."
Then there's reference to some work on the role of tranexamic acid, and there's a suggestion that that work be extended by a controlled clinical trial and, again, there is some further documentation in relation to that.
And there's a discussion halfway down that paragraph of dividing boys into two groups, one who would receive tranexamic acid for the first three days whenever they'd bled, plus Factor VIII replacement therapy, and the second group would merely be treated with replacement therapy alone.
Then it says at the end of that paragraph:
"This trial will need to be arranged so it does not interfere with any future trial of prophylactic therapy."
Then:
"In association with the laboratory study of therapy clinical observations will be made of the conditions of the boys with particular attention to the possibility of hepatitis. The work on hepatitis will be coordinated with that of Dr Craske of the Microbiology Laboratory at Bournemouth and with observations at Oxford."

Then the last page talks about the research fellow.
"Should the application for research support be granted, Dr Peter John Kirk has expressed interest in undertaking the research project."
Reference to appending his CV.
"We consider Dr Kirk to be quite unusually well qualified to profit by the research opportunity and ..."
And maybe you can read the next few words, sir, but I can't:
"... [something] of the exceptional facilities at the College, and at the ..."
SIR BRIAN LANGSTAFF: "... at the Oxford Centre."
MS RICHARDS: "... the Oxford Centre.
"It will be seen from Dr Kirk's [CV] that he has an excellent background for this research project. He has final qualifications in Laboratory Technology and is a qualified Medical Practitioner."
Then there's reference to him graduating from the University of Aberdeen in 1972, now taking his MRCP examinations.
"During his work as Senior House Officer at the Alton Haemophilia Centre Dr Kirk has shown great initiative, competence and responsibility and is

already engaged in many of the research projects at present in progress. These include the study of antithrombin levels in patients and the study of hepatitis.
"It is proposed that if Dr Kirk is appointed he should register as a student for the degree of Doctor of Medicine ... at the University of Aberdeen. We have every confidence he would obtain the degree in three years. Moreover we are sure that three years of research would be particularly beneficial to the future career of Dr Kirk who wishes to qualify as a Consultant Clinical Haematologist."
Sir, as I say, undated but clearly in the first half of the 1970s, given --
SIR BRIAN LANGSTAFF: Well, it looks though it is at a time when Dr Rainsford was bowing out to become part-time --
MS RICHARDS: Yes.
SIR BRIAN LANGSTAFF: -- Dr Kirk about to be appointed and is already working in the service at Alton. It also must be after '73 because there's reference to a '73 study in it. So it looks to be mid-seventies. Also it refers to viruses causing hepatitis, in the plural.
MS RICHARDS: It does, which might suggest 1974 or

thereabouts.
SIR BRIAN LANGSTAFF: '74, '75, probably, but it's very difficult to give an accurate date.
MS RICHARDS: Yes. I'm not sure we have a precise date for Dr Kirk's involvement. Not least because he had had some involvement in a house officer capacity already, so there are some earlier references to him. I'll check when we first see him referred to as a research fellow or assistant research fellow, to see whether we can give a more accurate date but it's roughly '74, possibly '75.
SIR BRIAN LANGSTAFF: Yes.
MS RICHARDS: Sir, I'm going to be looking at a number of documents in the course of the day, so perhaps now would be a good time for a break before I start.
SIR BRIAN LANGSTAFF: Yes, probably 11.50?
MS RICHARDS: Certainly.
SIR BRIAN LANGSTAFF: 11.50.
(11.18 am)
(A short break)
(11.50 am)
MS RICHARDS: Sir, with thanks to all those who assisted in relation to the date, the video that we looked at before the break is November 1987.
SIR BRIAN LANGSTAFF: November '87?

MS RICHARDS: That's what I understand.
SIR BRIAN LANGSTAFF: Right.
MS RICHARDS: Yes, there are lots of nods from the audience. Yes, November '87.

I've also been assisted over the break with the likely date for the letter from Dr Tomlinson that we looked at, September -- and then the year was unclear. I'm very grateful to the member of The Haemophilia Society who forwarded some information in that regard and suggested, and this sounds right, that it's probably September 1985 because it refers to media interest in a school in Hampshire, and it was in September 1985 in which there was some interest in precisely that topic.

So it would seem to fit that that would be September 1985.
SIR BRIAN LANGSTAFF: Yes. Thank you.
MS RICHARDS: Then to return then to some of the documents about research at Treloar's.

If we go back in time from the document we were looking at to 1970, AMRE0000012_004, we see here a letter from Dr Biggs in her capacity as director of the Oxford Haemophilia Centre supporting the continuation of funding for research at Treloar's. So the letter is dated 14 December 1970 and she says, in

relation to application from the Lord Mayor Treloar Trust, Alton, Hants:

"I feel this grant should be continued for a number of reasons:

"1. The collection of 49 haemophilic patients at the Alton School makes this a unique opportunity to study the disease."

So again, that way of looking at the pupils there which we've seen in really so many documents, here articulated by Dr Biggs.

"The patients are particularly important since crippling is still occurring and the question of prevention is under study.

"2. The work which Dr Rainsford has already done has defined the essential organisation required to treat boys gathered into one school. This was in itself a major research objective which has been achieved. As a result of this work and the efforts of local specialists and the Wessex Regional Hospital Board, a basic service for the treatment of the boys should soon be set up which will enable the Research Fellow to concentrate on purely research projects.

"3. In addition to the basic organisational research, Dr Rainsford has already initiated 7 other research projects, all of which are important, and

will cease if support for research is not forthcoming.

"4. Good cooperation has already been established between the work being carried out at Alton and the work of other research centres, particularly the one at Oxford, and we feel that it is most desirable for this cooperative work to continue.

"5. Although not specifically stated in this application, it is intended that Dr Rainsford should continue to as Research Fellow. Dr Rainsford has already shown himself to be an able organiser, to have many original ideas of his own, and to have immense energy and ability in obtaining cooperation from other scientists."

There is a little more information about Dr Rainsford's work at this time from AMRE0000011_066.

This a letter from Dr Rainsford himself, July 1970, and you'll see it was addressed, as was Dr Biggs' letter, to Mr Guthrie (and Mr Guthrie was the director of the National Fund for Research into Crippling Diseases) and Dr Rainsford says this:

"I think I ought to bring you up-to-date with regards to the research programme now being carried out here.

"In the original suggested outline of research six specific questions were posed ... about which,

with the exception of question three, conclusions had been reached by the time I was appointed. With regard to question three, epidemiological evidence here would appear to show that no beneficial advantage would be obtained from regular prophylactic injections, largely because of the short half-life of Factor VIII in the body.

"The present research program has been planned so that there should be no overlapping with that being carried out at Oxford. At present four separate research projects are being undertaken".

Then he gives details of those four projects.

"Project I: Epidemiological evidence collected here suggests that there is some seasonal variation in the tendency to bleed in both haemophilia and Christmas Disease."

So again, if we just skip down, we can see he says:

"It is thought that more evidence on these observations may be of fundamental importance and the plasma-cortisol levels of the boys suffering from these diseases is being routinely examined throughout the year."

We're told that's an investigation being carried out in cooperation with a Dr Shaw and Mrs Richardson,

consultant pathologist and principal biochemist respectively, at the Royal Hampshire County Hospital.

So that's project one. Project 2 involves -- and I'm picking this up from the third line of that paragraph:

"Sera ... is being examined for the presence of Rheumatoid Arthritis antibody ..."

And that is said to be:

"... a joint investigation, both clinical and pathological ... being conducted by Mr Stanley Evans, and myself. It is [described as] a fairly long term project and the relationship between Rheumatoid Arthritis antibody and the possible development of Inhibitors for Factor VIII is being studied."

If we go over the page, project 3 refers to a recent report about immunoglobulins in haemophilia, and Dr Rainsford says:

"This was discussed with Professor Nicholas Martin and Dr Rosemary Biggs and the serum of all our boys with haemophilia and Christmas Disease is being quantitatively examined for the immunoglobulins likely to be involved. These investigations may indicate those boys likely to develop inhibitors for Factor VIII ..."

And it's explained that that's a project being

undertaken in cooperation with Professor Martin and Dr Sharrard at the St George's Medical School.

Then project 4:

"Investigations carried out in conjunction with The Virus Reference Laboratory (Public Health Laboratory Service) with Dr Yvonne Cossart has shown that the incidence of Antibody to Australian Antigen is extremely high in our cases of Christmas Disease and Haemophilia. Dr Cossart has arranged to carry out regular examination of our cases for this Antibody and possibly to screen all the materials being administered for Australian Antigen. It is probable that much may be learned of the cause often serum hepatitis and its prevention could well be the outcome of these investigations. Furthermore, there is a serious shortage of sera for the detection of Australia Antigen in this country and the supply of sera from these boys will, therefore, greatly augment the present national bank of Australia Antibody sera, which will permit more widespread research into the relationship between the presence of Australia Antigen and hepatitis.

"Dr Biggs has approved this programme and all the projects are well under way."

That's an indication of some of the research

work being undertaken by Dr Rainsford in 1970, sir.

SIR BRIAN LANGSTAFF: Indeed, the Biggs letter from 1970, her support for Dr Rainsford, the way she is describing for those purposes how haemophilia -- boys suffering from haemophilia came to be at Lord Mayor Treloar's was because it was a research project.

MS RICHARDS: Yes. She refers to the organisational work undertaken by Dr Rainsford and --

SIR BRIAN LANGSTAFF: And she's saying well, Rainsford brought together a group of boys specifically to research them.

MS RICHARDS: That appears to be what she's saying, sir, yes.

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: Then we can see, if we go to AMRE0000007_002, an indication of some funding that was made available by what was subsequently renamed Action Research for the Crippled Child. I don't think there's a date on this letter but, in any event, it refers to an application having been received from Mr Evans, FRCS of the Lord Mayor Treloar Trust, for a grant of £24,815, but then we can see that historically some of the grant is made available. So:

"In July 1967, £10,000 was made available to the Lord Mayor Treloar Trust for a three-year

investigation at the Lord Mayor Treloar College and at the Blood Coagulation Research Unit, Oxford, of treatment of acute joint muscle haemorrhage in haemophilia."

Then:

"In January 1971. £15,000 was made available to the Lord Mayor Treloar Trust for continuation for three years of the grant for research into haemophilia.

I don't think this document tells us what happens to the further application that's referred to at the top of the page.

If we then go to AMRE0000011_021, this is a document entitled "Proposed Research Programme". Again, it's undated. We can tell that it's sometime earlier than August 1975 because there's a reference in the last page to that. The text of it is quite similar to the first document we looked at.

Sir, we see again, in the introduction, reference to Treloar College being a unique establishment because of the more than 50 boys suffering from various coagulation defects in residence there and under continuous medical supervision. And then we can see set out in the second paragraph, again, arrangements for the

treatment, which I think are largely a repetition of what we've already seen.

The third paragraph refers again to the Research Fellowship established in 1968, and it talks about it being unfortunate if the organisation was allowed to lapse for lack of financial support.

The next paragraph then says:

"It will be seen from the foregoing that the College lends itself to a specific type of research into haemophilia and other coagulation disorders, namely to study the relationship between recognised laboratory findings and clinical observations in these somewhat uncommon conditions. It is also the only establishment in the [UK] which can provide the opportunity and the facilities for extensive clinical trials of various kinds of treatment. This type of research cannot, at present, be conducted anywhere else."

Then there's a description under the heading "Future Research". If we go over the page, at the end of that long first paragraph, there's a reference to a proposed research programme. 1 is:

"Measurement of platelet activity and its relationship to factor VIII related protein and to determine whether the basic levels of Factor VIII and

its related antigen have any influence on the frequency of bleeding in haemophilia."

2 is:

"To determine whether the post transfusion levels of factor VIII and its related antigen has a bearing on the frequency of bleeding ..."

3 is in relation to fibrinolysis, and there's a discussion there again about the clinical trial and tranexamic acid; 4, antithrombin.

Then if we go over the page, we can see reference to "Completed Projects":

"1. A four-year study on the incidence of jaundice and the presence of Australia antigen and antibodies in boys being frequently transfused with blood products has now been completed in cooperation with the Virus Reference Laboratory, Public Health Laboratory Service, Colindale. Two interim reports concerning this project have already been circulated."

The second completed project is about plasma cortisol levels. The third is in relation to platelets, and then the fourth just refers to various other papers which are said to be of worldwide interest.

Then we have the heading:

"Current Projects.

"1. A prophylactic trial, to determine whether a prophylactic transfusion of Factor VIII administered at weekly intervals would reduce the frequency of bleeding in haemophilia, is now almost completed and a report should shortly be available."

2 refers to the ongoing research project:

"... to determine whether there is a relationship between immune arthritis and factor VIII antibodies ..."

There's reference, towards the bottom of that paragraph, to pre and post-transfusion samples of blood being examined by Dr Holborow at Taplow.

Then if we go over the page, and we can see that's to see whether there's some relationship to the development of kidney disease in haemophilia, and then we have the heading:

"Summary

"In proposing this future research it should be mentioned that the Area Health Authority has agreed to provide the Research Fellow with a full-time Research Assistant on a permanent basis for as long as a Fellowship exists. It must be fully realised that there is a limit to what the Research Fellow can accomplish with the help of one Research Assistant. It is, however, envisaged that the Centre, which is

now fully operational, well staffed and well equipped, will play a full part in assisting to carry out this proposed programme. It is considered that a fully trained and suitable candidate should be available in August 1975 to replace the present Research Fellow. This, of course, will depend on a three-year grant being made available, which would secure his future professional advancement to Consultant level".

This again appears to be looking at the recruitment of Dr Kirk to supplement to the work of Dr Rainsford.

Then:

"In addition, the Oxford Haemophilia Centre and the MRC Research Unit at Oxford have in the past assisted in all the research projects carried out at the College and it is assumed that this close collaboration with the proposed research work will continue. It will, therefore, be necessary for this Programme to be agreed, approved and sponsored by Dr PG Arblaster, Consultant Physician and Director of the Treloar Haemophilia Centre and Dr Rosemary Biggs, Director of the Haemophilia Centre and MRC Research Unit at Oxford."

Again, that's a broad update of the position as at the mid-1970s and, again, there's a letter a little

earlier, November '73, from Dr Biggs -- AMRE0000007_013 -- which makes clear the collaboration between Treloar's and Oxford.

So we looked at her 1970 letter of support to Mr Guthrie for funding for research. This is November '73, where she says:

"In my opinion the research already carried out at Alton has been of very great importance. The careful records kept by Dr Rainsford about the boys at Alton have been a great help in trying to estimate the requirements for the haemophilic community for Factor VIII, which is a very expensive therapeutic material. The projects proposed by Dr Rainsford are all in the first degree original and important. I have a very high regard for Dr Rainsford's ability in planning and carrying out his projects. In all the research work, very close cooperation has occurred between the Oxford Haemophilia Centre and those at Alton, and in some projects, advice has been taken from the Haemophilia Centre Directors Conference.

"In my opinion it is of the highest importance for research to carry on at Alton. The close cooperation between those working at the College and the Research Centre at Oxford is important and I believe certain to continue beyond Dr Rainsford's

tenure of the post. The work proposed is likely greatly to improve our knowledge of the distressing crippling caused by haemophilia".

Then there's a reference to the project in relation to rheumatoid arthritis. Then she says:

"I have no hesitation in supporting the application in full, particularly as I now believe that truly satisfactory arrangements are likely to be made for the day-to-day care of the boys at the college. I approve both the plan to extend Dr Rainsford's tenure until 1975 and the plan to seek a new Research Fellow for 1976 and 1977."

Sir, I'm going to look now, then, at some of the specific pieces of research and specific trials that were undertaken, starting with prophylaxis. We can -- there are multiple documents in relation to this, sir, I'm just going to just go to a handful.

We can start with DHSC0100026_146.

This is a letter dated 19 August 1972 from Dr Arblaster to a Dr Wilson, a principal medical officer in the Department of Health and Social Security, and he says:

"I would be most grateful if the Department would consider a research grant for a prophylactic trial in haemophilia, to be conducted by the Treloar

Haemophilia Centre.

"I enclose a copy of the Protocol which has been approved by Professor J Howell, Chairman of the Research Committee of the Wessex Regional Hospital Board.

"It has also been approved by a meeting of several haemophilia treatment centre Directors, held under the Chairmanship of Dr Rosemary Biggs, at Lord Mayor Treloar College.

"Some points need clarification ..."

Then there is the reference to:

"1. The request for £20,000 is for drug bill only. Current nursing, medical, and secretarial staff should be able to service the trial."

Then there is reference to terminology as between a "Switch Back Trial" and "Cross Over" trial in paragraph 2. It says:

"... each boy would act as his own control and where the trial duration is as planned, namely six terms, three would be prophylaxis and three terms placebo."

"3. The double blind method is suggested to exclude observer boys, and perhaps even more important, 'patient' boys. The haemophilia boys are great adepts at taking the mickey out of doctors and

conducting their own treatment to suit scholastic and social inconveniences!"

Then:

"4. The Ethical Committee of the North Hampshire Hospital Management Committee have considered the protocol in its earlier form, and I am sending the latest draft again today."

We can see there the request for financial support from the Department.

If we go to MRCO0000065_013, and we zoom in on the letter, we can see it's dated 10 January 1973, and it's addressed to a Dr Stewart at the Medical Research Council.

If we go to the bottom of the page we can see -- we'll see who it's from. From R Harwood in the Research Division of the Department of Health and Social Security. And then we can see it says in the second paragraph -- if we just look at the heading, first of all -- I'm sorry, Soumik -- under:

"Dear Mr Stewart,

"Trial of Factor VIII Concentrates at Lord Mayor Treloar College."

Then the second paragraph:

"The purpose of this letter is to give you formal notification that the Department will meet the

costs of the drugs used in the haemophilia trial of Factor VIII concentrates up to a maximum of £4,000 in 1973/74. I understand that no other research costs are involved. It is anticipated that the Trial will start in April.

"I note that the MRC [Medical Research Council] intends to set up a small group, on which DHSS will be represented to consider some revision of Dr Arblaster's protocol and if appropriate, to monitor the progress of the trial and assess its results. I take it that you will be in touch with Dr Metters about this. Time is short if the Trial is to begin at the start of the school term in April, and I know Dr Arblaster is anxious to begin."

Then we can see some further discussions about this trial.

HCDO0001015, please.

So this was a meeting of the Haemophilia Centre Directors in October of 1972. We can see Dr Aronstam was present as was Dr Rainsford.

If we go to page 5, there's a discussion about the protocol for a trial of prophylactic therapy in haemophiliacs.

"Dr Biggs said she had been asked at the last meeting to prepare a protocol. She had had a great

deal of trouble with it. She had sent it to number of important persons to see what they thought of it and they all objected to it for one reason or another. She concluded that it would be very difficult to organise a prophylactic trial from a Haemophilia Centre and that perhaps the only place where it could be done would be at Lord Mayor Treloar College. She had sent the protocol to Drs Arblaster, Aronstam and Rainsford (at their request) and they were now planning to organise a trial along the lines similar to those in the circulated protocol. Although there were difficulties in organising a trial and in the setting up of the control groups, Dr Biggs felt that it was very important for a trial to be undertaken because we really want to know whether the patients are better having prophylactic therapy or just receiving treatment 'on demand'. There were sharp differences between these two modes of treatment.

"On Demand Treatment means giving treatment at home or at hospital whenever a bleed occurred. Prophylaxis involves treatment at regular intervals regardless of whether or not bleeding occurs. Dr Biggs suggested that the Directors should support the conduct of this trial at the Lord Mayor Treloar College."

If we go over the page it appears that there was a lengthy discussion at the Haemophilia Centre Directors meeting about a prophylaxis trial, centering around three topics in particular of the placebo group, the material to be used, and details of the trial organisation.

There's then a discussion about the placebo in the following paragraph. It says in the fourth line:

"Some thought it very important that the placebo be indistinguishable from the treatment material since it was essential that the boys should not know to which group they belonged. It was however pointed out that the boys could be told that they were receiving two different treatments."

There's then a discussion about choice of material.

"It was decided that the trial material would have to be provided in addition to the material supplied for routine use at Lord Mayor Treloar College. The conclusion was that a freeze-dried concentrate should be used. Doctors Arblaster and Aronstam decided to use the Immuno material from Vienna if this was possible and had applied to the Ministry of Health and Social Security for £15,000 to buy enough material."

We have seen an exchange of correspondence in relation to the application to the Department of Health.

"It was pointed out that the Hyland concentrate was also of good quality. Also, Doctors Maycock and Bidwell thought that they could supply enough material were they asked [and that obviously would be NHS material]. Dr Biggs said she felt that any material which could be made in England was too urgently needed for treatment of serious bleeding for it to be allocated to a clinical trial of prophylactic therapy."

So it appears that the offer was made from Maycock and Bidwell for a trial of NHS concentrate for the prophylactic trial and the view expressed by Dr Biggs is, "Don't use it for prophylaxis on the children. Save that more generally for treatment on demand".

Then there's a discussion:

"About the organisation of the trial, questions were asked about the treatment of boys during holiday. The trial treatment would have to lapse during holidays and this was a pity. The frequency of dosage was discussed. Dr Matthews said that previous workers had advocated dosage varying in frequency from twice

daily to once every three to four weeks. It was decided that once weekly was the most frequently that dosage could be given in practice and that trial treatment must be allowed to lapse during holidays.

"It was stated that 10-15 boys could be included in the trial at Lord Mayor Treloar College. Some wondered if any significant results could be obtained with so few boys. It was pointed out by Dr Aronstam that each boy had many bleeds and that it was bleeding frequency which was to be used as the criterion of treatment effectiveness. Moreover, the boys would all have periods in the treatment group and in the control group. It was pointed out that since prophylactic treatment might treble the usage of factor VIII, only a highly significant result was of interest."

Then the last paragraph on this page:

"Co-operation of Haemophilia Centre Directors would be required wherever possible to obtain parents' consent for boys in the trial and to supervise boys in the holiday".

Then over the page under the heading "Action":

"In conclusion it was pointed out that details of this particular trial, including the choice of therapeutic materials and questions of ethics, were the responsibility of the Alton Centre and it was

proposed and agreed with one dissenting vote (Professor Stewart, Middlesex) that the Chairman should write to the Ministry of Health and Social Security supporting the conduct of the trial of prophylactic treatment at the Lord Mayor Treloar College. It was also agreed that the Haemophilia Society should be asked to make a contribution towards the cost of the trial."

That's the background and the discussion that took place amongst Haemophilia Centre Directors.

There are then a couple more documents I think of interest in relation to this issue.

So if we go to AMRE0000007_019.

Again, it's not a brilliant copy. We can see it's headed:

"Future Research.

"Observations made during the last four years at Lord Mayor Treloar College of boys suffering from haemophilia, strongly suggest that the frequency and duration of spontaneous bleeding are not solely a function of the presence of inadequate amounts of factor VIII in the blood. These observations indicate the following lines of investigation might be pursued."

Then there are various lines of investigation

discussed, a number of different research projects, you'll see paragraph 6 refers to the serum hepatitis project continuing at the request of the Public Health Laboratory Service.

Then we can see paragraph 7 talks about prophylaxis and this particular trial. It's not very easy to read but it says:

"At a meeting attended by the Directors of the various Haemophilia treatment Centres in the country held at Oxford on 27 October 1972 [so those are the minutes we've just looked at], it was unanimously agreed that a Clinical Trial to evaluate prophylactic therapy in the treatment of Haemophilia should be carried out. It was decided that it should take the form of a double-blind cross over trial and a protocol for such a trial was drawn up by Dr Rosemary Biggs and discussed. It became obvious after discussion that such a trial could only be pursued at an establishment like Lord Mayor Treloar College where boys are under close daily observation for prolonged periods and where meticulous day to day records on each boy are maintained. Primarily this is due to the organisation already set up by the Research Fellow and his secretary, the cost of which is covered by the grant from the National Fund for Research into Crippling

Diseases. Now that this organisation is established, the Lord Mayor Treloar College is an ideal centre for this type of research and in this respect it is unique in this country. It would therefore be a pity if such an organisation was allowed to lapse for lack of financial support."

Then it refers to the Ministry of Health having agreed to cover the cost of materials. It has the formal approval of the Medical Research Council.

"Much time and trouble has been spent by the Director of Lord Mayor Treloar Haemophilia Centre and his Deputy in the detailed planning of this trial. Boys to be included in this trial had to satisfy certain strict criteria and were selected accordingly by the Research Fellow. The trial commenced during the Summer Term of 1973 and it is not likely to be completed before the end of the Spring Term 1975.

"This trial is one of the most important research studies now being carried out in this county [I think it says, or 'country' might make more sense] on the treatment of haemophilia and its implications could be profound."

Then if we go to MRCO0000065_022.

This is an observation by I think someone in either of the Department of Health or the Medical

Research Council on the meeting and the discussion that took place at the meeting in October '72, so it's a note or a memo dated 8 November 1972.

"I attended the meeting of the Haemophilia Centre Directors on October 27th. Several of the agenda items were of interest, but one in particular has special reference for us -- the proposed trial of prophylactic therapy.

"Dr Biggs had been asked by the equivalent meeting last year to produce a protocol, and it was this that was debated. A subsequent (mark 2) version of the protocol has been sent to DHSS and it is the mark 2 version that we have received from the Department of Health and Social Security."

That would suggest this a medical research counsel note.

"Dr Biggs said it was clear that no individual Haemophilia Centre could organise a trial of this type -- for ethical reasons apart from anything else -- but the Lord Mayor Treloar College at Alton were able to undertake it, and any other centres who could do so were welcome to join."

Just pausing there, it's not clear from any of this material why it's thought that ethically it's problematic to conduct this work elsewhere but it's

ethically acceptable to conduct it at Lord Mayor Treloar College on children.

"Several points concerning the designs of the trial were discussed, and it became apparent that some of the Directors present either had reservations about it or disagreed with particular points. Dr Maycock was asked whether the Plasma Fractionation Laboratory or the Blood Products Laboratory would be able to make the required amounts of Factor VIII concentrate, as this might provide a considerable saving compared with buying such concentrate from a commercial firm in Austria at a cost of £15 - 20K. Dr Maycock replied that he saw no difficulty in producing the material if the appropriate financial assistance and sufficient fresh frozen plasma was available. This statement caused some lively discussion, and it was clear that if more Factor VIII concentrate really did become available from PFL or BPL, the Haemophilia Centre Directors would want to use it for treatment rather than in a clinical trial. Dr Maycock pointed out, however, that it might be possible to increase production, given the necessary raw materials and funds, on a continuing basis rather than having to spend the available finance on one single batch of Factor VIII.

"In discussion with Dr Biggs, Dr Maycock, Dr Arblaster, and Dr Aronstam I discovered that all the objections raised by the Haemophilia Centre Directors had already levelled at the protocol, and the version which had been sent to the DHSS took account of them so far as possible. The DHSS were apparently sent the protocol many months ago, and the people who hope to run the trial clearly now are relying on the Council to speed up the process of decision.

"There seemed to be two main issues -- first, should a trial of the type described be carried out, and second, should Factor VIII concentrate be provided through Dr Maycock and Dr Bidwell or from commercial sources. I think there is a case for the Department deciding both these questions in general terms and then the Council to play some part in perfecting the design of the trial and becoming involved in an advisory capacity."

And so there is quite an illuminating insight from the attender from the Medical Research Council at the Haemophilia Centre Directors meeting on the discussions and the concerns that were being expressed about the trial and the question of what product to use.

There is also a discussion of the trial at TREL0000521.

This is a meeting of the research sub committee of the Wessex Regional Hospital Board, 8 February 1973. If we go to the bottom of the second page, there is a discussion of the prophylactic trial in haemophilia:

"The Committee received details of a proposed trial to be carried out at the Lord Mayor Treloar Hospital, Alton, under the direction and control of Drs Arblaster and Aronstam, to establish whether or not the use of Factor VIII material would reduce the incidence of bleeding in haemophiliacs".

Top of the next page:

"Following discussions with the Chairman, this proposal had been sent to the Department of Health and Social Security, with the Board's support, and a request made for funds to finance the research over a period of three years.

"The Department of Health had now written to say it was willing to make available £4,000 for the trial, which would be carried out at Alton and a small steering committee was being set up by the Department of Health and the Medical Research Council to advise on the protocol and suggest further revisions to the

trial plan where this could be done with advantage. The funding of this project will be arranged by the Department of Health direct with the North Hampshire Group.

"The Committee noted this development with satisfaction."

Sir, unfortunately, that doesn't cast any further light on the question of consideration of ethical implications.

If we go to MRCO0000065_011.

We zoom in again, it's not always easy to read this. Sir, we can see:

"Trial of Factor VIII concentrates at Lord Mayor Treloar College.

"Record of a meeting held at 20 Park Crescent ... 9th March 1973 ...".

Sir, this appears to be a Medical Research Council meeting, I think. We can see present Dr Arblaster, Dr Aronstam, Dr Rainsford, as well as Dr Bidwell, Dr Metters from the DHSS, Dr Stewart from the MRC and Dr Bunje, chair, who I think one of the earlier memos we looked at was addressed to. Then we can see:

"[The chair] summarised the events that had led up to the meeting and suggested that the role of the

MRC might prove to be simply to bring together those people who could contribute to the design and conduct of the proposed trial, and to ensure that adequate arrangements had been made for its organisation and the assessment of results. He suggested that discussion might conveniently be directed to the following four subjects:

"1. The trial protocol.

"2. Consideration of matters relating to children involved in the trial.

"3. Consideration of matters relating to the Lord Mayor Treloar College.

"4. Financial aspects."

Then if we go to the discussion of the trial protocol, to the bottom half of the page, we can see it records Dr Rainsford saying that the proportion of clinically severely affected children at the college was about 25%. Then there's a discussion of the proportion in the population at large.

Then the next paragraph says:

"At the present time there were only 8 boys at the college who fell into the 'severe' category. Dr Aronstam pointed out that the significance of the results would not be dependent upon only the number of boys in the trial but also perhaps the total number of

'bleeds'. In order to answer criticisms of the significance, the trial could be extended by a year (or whatever time was appropriate) or the college could accept more boys."

So there's a suggestion there potentially, or one inference that one might be drawn of recruiting boys to the college so that this could be a trial of greater clinical and research significance.

"The limitation was not the number of boys who would be accommodated but the availability of the Factor VIII material."

Then we see the chair suggesting:

"... that the trial should be continued until at least 15 boys had been included and the results should then be examined with a view to assessing their significance. It was agreed it would not be possible to have 15 in the trial concurrently since the resultant laboratory workload would be too heavy, but that the trial could be lengthened as required. Dr Bidwell confirmed that, as far as could be foreseen, Factor VIII could be provided in sufficient quantity over the period of the trial.

"It was agreed that the criteria of eligibility for the trial could not be changed for combination of ethical, statistical and practical reasons ..."

Again, it's not clear what the ethical reasons are.

"... and it was agreed that the trial would be continued, with continuous assessment of the significance of the results, for as long as necessary."

There's then a discussion about the number of bleeds that one would need in order to be included in the trial. The last sentence of that paragraph:

"If the trial was successful ..."

Sorry, can we just go up again, Soumik.

"... the use of Factor VIII might be extended to those with lower frequency of bleeding."

Then there's a discussion about various aspects of the arrangements. The penultimate paragraph on that page says:

"Dr Arblaster reported that a letter for parents had been prepared but that it would not be sent out until all the other arrangements for the trial had been confirmed."

Then there was a discussion about taking samples on each boy, and to confirm Factor VIII levels, at the bottom of the page. If we go over, we can see the conclusion of the discussion:

"Costs. Dr Bidwell pointed out she could not

readily assess the cost of producing Factor VIII in financial terms."

She is said to be able to manufacture the additional Factor VIII required:

"... provided the number of boys in the trial was never more than 10 ...

"Dr Aronstam said that the extra time that the technicians in his ... Department would require would be organised locally."

So this meeting appears to be contemplating, contrary to what we saw in the Haemophilia Centre Directors discussion, that there would be a supply of Factor VIII for the trial from Dr Bidwell.

We've got various documents associated with the trial but it's not possible often to tell whether they are early versions of documents or final versions. I'll just look at one example, therefore.

MRCO0000065_021.

So this is -- it's headed:

"Study of Preventative Treatment in Haemophilia.

"A Controlled Trial.

"Data Forms.

"Determination of Patient Eligibility."

If we go to page 3, we can see the criteria for a patient to be eligible:

"Does the patient have ... classic haemophilia with ... a compatible family history and ... a factor VIII level of 1% or less?"

If no, then "stop", so they're not eligible.

"Is the age of the patient 7 years or greater?"

So that's the cut-off, 7-plus.

"Is the patient a male?

"Has the patient a bleeding frequency of 7 episodes per 100 days during the past two school terms?"

If yes, eligible for inclusion, if no, they're not.

"Does the patient have Factor VIII inhibitors?"

If yes, they are not eligible for inclusion.

"Is an elective surgical, orthopaedic or other procedure planned which would interfere with the proper execution of the trial?"

If yes then, again, we see "stop", so not included.

"Will the parent be participating in school studies with requirements in conflict with those of this trial?"

Again, if yes, it's stop.

"Have the patient and his parents (or guardian) given their informed consent to participate in, and

fulfil the requirements of the trial?"

Again, that's seen as a requirement for eligibility. The answer is, if the answer is no, then they're not to be included.

"Is all the information on this data form recorded fully?"

So that's the form.

As I say, there are other versions of this document, but which chart a similar effect and it's not clear which is the final version but there is no marked difference between them for present purposes.

Then there's one -- again, one further document. DHSC0100026_147.

I'm not going to go through all of this. Again, it is not clear what the date is unfortunately. But it's a discussion about the study, so prospective study of preventative treatment in haemophilia.

We can see in the third paragraph it observes:

"The effects of prophylactic administration of Factor VIII concentrates may be complex. For example, a patient may gain sufficient assurance from such treatment as to ignore symptoms which would ordinarily cause him to consult his physician. Conversely, he may be prompted to exert himself more strenuously than he might otherwise, and thereby provoke a bleeding

episode. The effects of psychological influences on bleeding in haemophilia have been stressed ... It would be desirable to control these sources of potential bias by designing a trial with two specific requirements. First, the variation among patients might be controlled by a 'switchback design', whereby each patient serves as his own comparison. Secondly, the individual variation of a single patient between placebo and factor VIII might be controlled by employment of a double-blind method."

Then we can see, over the page again, the virtues of Lord Mayor Treloar College as "an ideal location" for the treatment are extolled.

"An ideal location for carrying out a clinical trial to evaluate prophylaxis would be a Centre where a relatively large number of severely affected haemophiliacs are closely observed daily; where the 'baseline' bleeding habits of the patients are known; and where personnel and facilities exist for separating clinical management from trial administration. Such a location is the Lord Mayor Treloar College."

Then we can see a discussion of eligibility criteria. I don't propose to go through the details of that, save to note that point 8, is:

"All patients must give their informed consent as defined below, prior to the final determination of eligibility."

If we go, then, to the next page, we can see a heading:

"Trial Design.

"The trial for an individual patient will consist of four school terms. During two of these terms, the patient will receive once-weekly infusions of freeze-dried Australia Antigen-screened factor VIII concentrate, and during the other two terms, once-weekly infusions of distinguishable placebo.

"The designation of these terms as treatment or placebo periods will be made on a random basis."

Then it talks about it might be necessary to delay treatment periods and the total trial period shall in no instance exceed six school terms.

Then in terms of obtaining of consent, if we look at the bottom, towards the bottom of the page, "Division of Responsibility", point 1 says:

"It is hoped that the Medical Directors of Haemophilia Units in the boy's home area will be responsible for obtaining consent for inclusion in the trial."

So it appears to have been contemplated that

Treloar's would not itself obtain consent but would leave it to the home clinicians to do so.

If we go over the page, there's then a discussion of the respective responsibilities of Dr Rainsford and Dr Aronstam.

Dr Rainsford was going to be blind to the treatment assignment. Dr Aronstam would be responsible for trial administration.

There is, if we look at paragraph 4, reference to Dr Tomlinson participating:

"The physician responsible (Dr Tomlinson and Staff) for therapeutic infusions, will administer concentrate or placebo to patients."

So that's an oddity, given what the evidence elsewhere suggests about Dr Tomlinson. But in any event, we then have the heading "Informed Consent":

"After tentative determination of a patient's eligibility, the trial will be explained fully to the patient and the patient's parents or guardian. The following points will be made clear:

"1. During the entire trial, each patient will receive an infusion once weekly of either concentrate or placebo.

"2. The patient will not be told to which treatment he is assigned.

"3. It must be understood that the only safe assumption for the patient to make, is that he is assigned to the placebo group. He should act accordingly by not taking undue risks, and by promptly reporting symptoms suggesting haemorrhage, as usual."

Top of the next page:

"4. All patients will receive best available treatment, as usual, for bleeding episodes when they occur."

And:

"5. Patients must agree an intention to participate in the trial for a full four terms."

Then there's a further discussion about the administration of the concentrate and so on.

So it appears to have been certainly built into the protocol that informed consent along the lines there discussed would be required.

You will note that in terms of the matters that are said to be necessary to make clear to patients, there is no discussion of possible risks of receiving prophylactic concentrates, in other words, receiving more concentrates than might otherwise be required for treatment of bleeding on demand. So any possible enhanced risks of viral infection with hepatitis, for example, are not there identified.

SIR BRIAN LANGSTAFF: Well, if we go back a couple of pages, at the bottom of the page, what do we make of that?

MS RICHARDS: We're told the placebo will be a hepatitis-free human plasma protein fraction, and is going to appear indistinguishable from the concentrate, but we're not told the concentrate is hepatitis free.

SIR BRIAN LANGSTAFF: So we know that is hepatitis free at least, at least free of hepatitis B, presumably.

MS RICHARDS: In terms of the placebo, yes. And we're told it's going to be, in terms of the actual concentrate, absolutely, we're told it would be Australia antigen screened. But of course, leaving aside any question over the adequacy of screening for hepatitis B, for Australia antigen, there is the broader question of other forms of viral hepatitis.

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: So those are some of the background documents underpinning the prophylactic trial.

Other evidence that we've got suggests that the trial did indeed commence in the summer of 1973. We have got one example, it may not be the only example, but it's one example we've got available for display, of a discussion by the home clinician with a parent.

TREL0000318_012.

Sir, this is a letter from a doctor based at the Warwick Hospital addressed to Dr Aronstam, April 1973, and it says in the second paragraph:

"During these holidays I have had an opportunity to discuss the research project using Factor VIII concentrates with [the patient] and his mother and they have agreed to cooperate."

There's then an update about the patient's condition, and then the last paragraph says:

"[The patient] has not had an episode like this for some years and it is very much to be hoped that the new preventative treatment will bring his coagulation time under better control."

That read with the earlier paragraph tends to suggest that this was a discussion about participation in the prophylactic trial.

So it would indicate that there has been a discussion with parents, and pupil, but it doesn't tell us what the substance of that discussion was, or what information was provided.

If we then look at a short update to the Haemophilia Centre Directors in early '74 on the trial, it is at CBLA0000187.

Sir, this is the minutes of a joint meeting of

directors of Haemophilia Centres and blood transfusion directors, 31 January 1974. Dr Arblaster, Dr Aronstam, and Dr Rainsford were all in attendance. There's a brief update at page 4 on the prophylaxis trial. So it's paragraph:

"(c) Trial of prophylaxis at Alton - an Interim report:

"Dr Arblaster described the aims of the trial and outlined some of the practical difficulties which they had come across early in the trial."

Minutes don't reveal what they are.

"Dr Aronstam then described the results of the first two terms of the trial. He stressed that the trial was still 'double blind'."

Before leaving this document if we look at the previous page, and this is just so I don't have to come back to the document, there is reference in the bottom half of the page to a survey of Australia antigen in household contacts of haemophiliacs, and we've seen reference to that previously. But we can see that there is, following a report from Dr Ingram, it says:

"Discussion about this paper included the following topics ...".

And then paragraph (iii):

"A report was made of the tests made at the Alton Centre (Dr Rainsford)."

So it appears that there was also participation by the Treloar's centre in this ongoing survey of Australia antigen in the household contacts of haemophiliacs that we know was being undertaken under the auspices of the Haemophilia Centre Directors at this time.

If we then pick up the progress of this trial at NHBT0107241.

This is one of the termly reports that we've previously looked at. This is authored by Dr Rainsford in January 1975, and it's reporting on the summer term 1974 and the autumn term 1974. We looked previously at what was said at the bottom of page 2 and 3 about the hepatitis outbreak. If we go to page 4, we see reference to the "Prophylactic Trial". So under the heading:

"Research Programme

"Prophylactic Trial - This trial is now complete and a report is being prepared.

"A new research program to cover the next three years has been formulated and acceptance of this programme is awaited from the National Fund for Research ..."

Then we can see reference to preliminary work on that and other projects, including the hepatitis project.

So if we look further down we see the date, January '75. We're told that prophylactic trial has been completed.

Then if we pick matters up in the Haemophilia Centre Directors meeting of September 1975.

OXUH0003735.

We see the date at the top of the page, 18 September 1975. Dr Aronstam, Dr Kirk and Dr Rainsford are all present. If we go then to page 8, we can see towards the bottom of the page an update about the trial of prophylactic treatment.

"Dr Aronstam gave a report on the trial of prophylaxis at the Lord Mayor Treloar College at Alton. He presented the data which was being prepared for publication. He said that there was evidence that the boys in the treatment group were protected for 48 hours following a dose of factor VIII. Dr Aronstam said that he had encountered difficulty in organising the trial, and felt that an extension of the trial should not include a placebo dose."

Then there's a discussion, following an intervention from Dr Cash, that prophylaxis could

result in an annual dosage of more than 70,000 units of Factor VIII per patient per year. Then someone else points out that:

"... quite small doses were often effective for 'on demand' therapy and that even less might be required for prophylaxis. Dr Stewart proposed that the trial be continued on a regime of two doses a week at 2 dose levels ...

"ACTION. It was agreed to recommend that the trial be continued at 2 dose levels."

Then I will come back to this -- actually, whilst we're here, we might as well pick it up here. There's a discussion of two other aspects of research being undertaken at Treloar's at this time. The continuation on this page refers to a proposed pilot study of hepatitis in haemophilic patients and I'll come on to that this afternoon, but you'll see Dr Kirk is referred to as introducing a paper on a proposal:

"... to study the incidence of hepatitis in haemophilia patients who have received material of known types. He was proposing, as a pilot study, to keep detailed records on the following patients ..."

Then we see a reference to Treloar's, Newcastle, and Oxford. I'll just concentrate on Treloar's:

"At Treloar College, 20 patients receiving

cryoprecipitate, 10 patients receiving Kryobulin and 5 patients receiving Elstree Factor VIII."

The bottom of the page says:

"Any Director who would like to contribute to the Study should contact Dr Kirk at Lord Mayor Treloar College ... A requirement for participation in this trial is that a patient should receive only one type of material for treatment and that samples for virology testing be collected and sent to Dr Cossart at the Virus Reference Laboratory.

"There was some discussion about the collection of samples for LFT and virus testing and it was felt that it was important to arrange for as many tests as possible but it was also felt that frequent testing of patients, particularly those on home therapy, could be difficult. Therapeutic material should be saved for virus testing in case new types of test were developed."

You may wish to note, sir, that it appears to have been regarded as something that could be achieved for research purposes to keep a patient on one type of concentrate for the purposes of research, but more broadly for the purposes of treatment, we've seen that wasn't the approach that was taken.

And if we go to page 4, there's a further

discussion about hepatitis and liver function tests in the bottom half of this page. This is in the context of the directors' study of jaundice and Factor VIII antibodies. It says:

"There was a full discussion about the incidence of hepatitis and the problem of anicteric cases."

Then -- sorry:

"Prof Stewart thought that the cases of hepatitis should be more precisely defined according to the criteria on which the diagnosis was made."

Then we can just see a slight difference of approach between Dr Kirk and Dr Rainsford:

"It was felt that future statistics should include [liver function test] results ..."

And that's said to be the view of Dr Craske and Dr Kirk:

"... though others felt that [liver function test] results were often said to be difficult to interpret ..."

And that's said to be the views of Dr Maycock and Dr Rainsford.

In any event, there we have an update on the prophylaxis trial.

If we go to MRCO0000065_005.

SIR BRIAN LANGSTAFF: Just before you do, the last five

lines there.

MS RICHARDS: "Professor Ingram" -- sorry:

"The influence on the pool size of material used for fractionation was discussed, Prof Ingram said that NHS Factor VIII was derived from pools of 500-750 donations whereas the commercial factor VIII was often derived from pools of 2,000 to 6,000 litres of plasma and that the probability of including an infected donation was greater ..."

Top of the next page -- sorry, do you need the -- OXUH0003735. And if we go to the top of page 5.

"... was greater with commercial factor VIII."

Then there's a discussion about not issuing for use material that was hepatitis B antigen positive.

Is that the passage to which you were referring to, sir?

SIR BRIAN LANGSTAFF: Yes, thank you.

MS RICHARDS: Sir, then if we just go to MRCO0000065_005. And if we can zoom in, it's very difficult to read.

Sir, this is a letter from Dr Aronstam to the Medical Research Council, 22 July 1975. We can see it's headed "Prophylaxis in Haemophilia", and he says:

"You may remember Chairing a meeting at the Medical Research Council three years ago when we

discussed the protocol for a double-blind controlled trial of prophylactic therapy in haemophilia. Dr PG Arblaster, who is now in Arabia, and myself together with Dr Rainsford attended for the Treloar Haemophilia Centre where the trial has been carried out.

"We have now gone as far as we can with this trial in the face of, I may say, enormous difficulties which I feel were a direct result of using a placebo for this study.

"We have had to make some modifications to the original protocol but nevertheless I believe our final report, a copy of which I enclose, has done what we set out to do - that is to establish that prophylactic therapy actually works."

We can see a published paper on the trial at NHBT0000091_036:

"Prophylaxis in Haemophilia: A Double-blind Controlled Trial."

It's reported in the British Journal of Haematology in 1976 and we can see it was received for publication in July '75.

I'm not going to go through the detail of the report because it's -- well, it's several pages long and it would be -- I think take a disproportionate

amount of time. But we can see:

"Summary: A double-blind controlled trial of prophylactic factor VIII therapy has been carried out on nine severe haemophiliacs at the Lord Mayor Treloar College. Infusions were given once weekly and calculated to give a post-infusion plasma concentration of at least 0.25IU/ml of factor VIII."

Then it's said to have reduced the overall bleeding frequency by 15%.

"The bleeding frequency in the first 3 days post-infusion reduced by 66%. A moderate overall reduction in morbidity was also achieved. It is calculated that to reduce the incidence of bleeding in severe haemophiliacs by 15% would require a 73% increased usage of therapeutic materials. More than twice this amount of material is likely to be needed to reduce the bleeding frequency of the same group by 66%."

Sir, that's a summary of the findings. I've just looked very briefly at a couple of pages, second page, under the heading "Materials and Methods", describes how the trial was conducted. We can see the "Eligibility Criteria". The third paragraph asserts that:

"The nature of the trial was fully explained to

the eligible boys and their parents or guardians were asked to give their consent; if this was obtained the boy was admitted to the trial."

As we've seen, the indications from the documents are that that was a process, as it were, delegated to the home clinicians, home treating clinician, rather than directly undertaken by the clinicians at Treloar's.

Then there is a description on the following page of each of the nine boys. Then, if we go over to the fourth page, we can see set out there the results in both tabular and narrative form:

"Nine boys studied for a total of 27 boy-school terms ... Ninety-seven infusions of high-dose and 95 of low-dose material given."

Then if we go to page 7, we can see "Development of Inhibitors":

"No case of an inhibitor ... developed during the trial ...

"No case of hepatitis associated antigen developed during the trial, although one boy ... developed antigen negative hepatitis 23 [days] after entering the trial. He was withdrawn for the remainder of that term."

Then the discussion is probably something that

merits reading in full by you, sir, rather than me simply reading out.

SIR BRIAN LANGSTAFF: Yes.

MS RICHARDS: But it talks about what might be required by way of dosage in order to achieve therapeutic benefit.

If we go over the page, the last paragraph refers to problems in the trial, maybe what Dr Aronstam was referring to earlier when he described practical difficulties in the trial, or it may not. It said:

"Some bleeds were bound to occur shortly after infusions of low-dose material and sooner or later a crop of bleeds will occur. On one occasion four boys were together in the sick bay within 24 [hours] of a low-dose infusion. They concluded that the material was the cause for their bleeding and it was difficult to persuade them to remain in the trial. Two, in fact, dropped out soon after this episode. The giving of a dose interferes with a boy's leisure and schooling and when inert material is given [so placebo] this may not be easily justified. In our view, future trials should compare only probably effective prophylactic regimens and should not include placebo doses."

So that's the first trial of prophylaxis. I'm

not going to go through the same level of detail in relation to the other trials of prophylaxis because really we've seen the groundwork and the framework in the documents we've looked at, and the involvement of the Department of Health and Medical Research Council.

But we can see, if we go to RLIT0000084, a later publication:

"Twice weekly prophylactic therapy in haemophilia A", reported in 1977, so this is a later trial of prophylactic treatment, and the summary tells us that:

"Factor VIII-containing materials were administered to four severely affected haemophiliacs twice weekly in doses calculated to raise the Factor VIII level to either 15% or 30% of average normal."

Then it suggests that the results from the patients show the reduction in -- a significant reduction in bleeding frequency on both doses in the first 48 hours and so on.

If we just go back to the text on this page, the first paragraph refers to the previous prophylactic trial, and then, if we pick it up at the bottom of the left-hand side of the page, please:

"In view of the implications for the limited

financial and human resources available to service such a commitment, it is important to confirm these findings [so the findings of the earlier trial] and to establish the lowest dose which might be beneficial. The work reported here is a step along that path."

So this was seen as building upon the prophylactic work previously undertaken.

Details are given on the second page of the trial design. And if we look at the bottom of the page, we see the heading of the left-hand side "Prophylactic Materials." We can see that this was a trial that involved cryoprecipitate, apparently, but also involved Kryobulin.

And then we'll just look at the last page under the heading -- oh, I'm so sorry, the page before that.

So there's a heading, "Discussion". If we go to the right-hand side, I pick it up in -- sorry, the top half of the page, right-hand side. Second paragraph:

"From the data presented it might reasonably be concluded that the 24-hourly prophylactic administration of a dose of factor VIII, calculated to raise the level to 30% would reduce the bleeding frequency by 90%. The application of a similar calculation to that explained above suggests that such a commitment would need nearly nine times the amount

of therapeutic material currently in use for haemophiliacs with comparable bleeding frequencies.

"Clearly, this sort of commitment is not possible with known therapeutic materials, given the current limitations of human and financial resources, particularly in the UK."

Then we can see that the authors then say that they think:

"... further work in this field should be directed towards the possible benefits of limited periods of prophylaxis."

So that's the next, as it were, step along the line of investigation of prophylaxis undertaken at Treloar's.

Sir, I'll just mention, then, that there was then a third trial of prophylactic treatment. That did indeed, as anticipated here, look at short-term prophylaxis and whether that would reduce bleeding frequency, and we know -- and I won't go to the documents in relation to this third trial, but we know that the therapeutic material used for that trial included cryoprecipitate, NHS Factor VIII, and commercial Factor VIII. And it was conducted between 1976 and 1977, with prophylaxis being administered twice weekly to five boys and three times weekly to 13

boys.

If we could just go to the very final document of relevance, I think, on that third trial, it's Dr Kirk's update to the Haemophilia Centre Directors.

PRSE0002268.

So it's a meeting of Haemophilia Centre Directors January 1977. If we go to page 9, I think. Yeah, bottom of the page. We see reference to:

"Trial of prophylactic treatment of haemophiliac patients at Alton ... Dr Kirk reported on the third trial of prophylactic treatment at Alton, the aim of which was to see if prophylactic treatment reduces the incidence of bleeds in severely affected haemophilic boys. All patients in the study already had bad joints."

Now this records treatment with cryoprecipitate, Kryobulin and Hemofil, but there are other documents that suggest NHS concentrate used.

Sir, I'll check the final published report to see if it clarifies that.

Then we can see over the page there's then a discussion about the use of prophylaxis. About halfway down that long paragraph there's a reference to:

"Dr Blecher [asking] which regime the boys

preferred - on demand or prophylaxis. Dr Kirk replied that the 2 boys with the best results ... wanted to stop prophylactic treatment; the others wanted to go on. Possibly the 2 boys with good results had forgotten what a bad bleed was like. Prof Stewart felt that prophylactic treatment for haemophiliacs should not be entered into on a large scale until there was sufficient evidence that it was beneficial to the patients. Dr Rainsford said that the prophylactic trial was aimed to provide information for the future and not with the intention of immediate implementation."

So you'll see there some reservation being expressed by some directors as to whether this -- well, as to whether this was an appropriate way in which to treat patients.

So that, I think, brings me to a convenient point at which to break for lunch.

SIR BRIAN LANGSTAFF: Yes. We will take a break until two o'clock. Two o'clock.

MS RICHARDS: Thank you, sir.

(1.03 pm)

(The luncheon adjournment)

(2.00 pm)

MS RICHARDS: Sir, just to complete the picture in

relation to the publications regarding the trials of prophylactic therapy, the third trial was written up in RLIT0000093:

"Transfusion requirements of adolescents with severe haemophilia A."

Aronstam, McLellan and Turk.

I'm not going to it in any great detail but if we'd look at the bottom of the page, right-hand side, under the heading "Patients and methods", we can just see it says:

"Seventy-five boys without inhibitors and with haemophilia A were studied during the years 1973-77."

The next paragraph talks about third trial, so:

"Prophylactic Factor VIII given to 15 of the boys for limited periods during 1976 and 1977. Prophylaxis was administered twice weekly to five boys during 1976 and three times weekly to 13 boys during 1976 and 1977."

Then the publication clarifies what products were used, so bottom of the page:

"Each transfusion was of cryoprecipitate, [NHS] factor VIII concentrate, or commercial factor VIII concentrate, and was recorded as a single transfusion irrespective of dose."

I don't think this document tells us which

commercial concentrates were used, so we may need to fall back on what was said in the earlier documents in that regard.

So that's the third trial of prophylactic treatment. There's one further document I'd like to refer to on that but we haven't yet got it available for screening, so I'll come back to that. I'm going to move then to one of the other major areas of study and research which was the hepatitis study. It was often referred to as such but, in fact, it is probably better regarded as a series of studies carried out over a number of years.

If we go to HHFT0000053_001, we can see this is entitled:

"The Incidence of Australia Antigen and Antibody in boys suffering from coagulation disorders.

"Report of a Study at the Lord Mayor Treloar College."

It is authored by Dr Rainsford and Dr Cossart and it tells us that:

"Each year as many as 50 of the disabled boys attending the Lord Mayor Treloar School are suffering from haemophilia or other coagulation defects. This concentration in one residential of centre of patients needing repeated transfusions has provided a good

opportunity to study the incidence of Australia antigen and antibody in a vulnerable group."

You'll note the words there used.

"The original plan was to follow the pattern of antigen and antibody in the boys and to relate these findings to clinical illness, frequency of transfusion and the presence of Australia antigen in the blood and blood products with which they were treated. It was hoped to test the boys each term and to test an aliquot of the blood, or pool of blood products, given in each transfusion".

Then reference to various tests.

"The study has continued for 10 terms (Summer 1970 - Summer 1973).

"81 boys have come under observation, 71 haemophiliacs (11 with inhibitors) and 7 with Christmas Disease, 2 with von Willebrand's, and 1 with aplastic anaemia. 20 have been at the College throughout the study, but it has not been possible to examine the blood of every boy every term because of hospital admissions. The collection of samples from boys needing very frequent transfusion has been difficult because it was thought undesirable to test sera obtained less than a week after transfusion."

Then we can see reference in the top half of the

page to, in one particular period of time, examining the transfusion samples, and then it's recorded in the next paragraph that:

"Since the Spring term 1971 the Wessex Regional Transfusion Centre has been screening all donors supplying material for the treatment of these boys ..."

Screening for Australia antigen.

There's then a reference to the results. In terms of antigen, the position of three boys described. In relation to antibody, again, there's a description of the antibody results. If we go to the next page, bottom half of the page. There's a heading:

"Relation of Australia antigen and antibody to hepatitis", and there's references to some attacks of hepatitis and jaundice.

If we go over the page, we can just see the "Summary and Conclusions":

"Three of the 81 boys with coagulation defects were Australia antigen positive at some time during the survey. One was a persistent carrier ...

"Thirty five to forty per cent of the boys were antibody positive at all stages of the study. As antibody is evidence of previous exposure to serum

hepatitis, it probably also indicates immunity and it is not surprising that clinical hepatitis is uncommon in adult haemophiliacs.

"Although the amount of antigenic stimulus in the transfusions given after screening began was less than before, it is still significant."

Then we're told that:

"Only 12 of the 81 boys had suffered clinical attacks of hepatitis, although most had frequently been transfused since infancy. It would seem that exposure to antigen positive blood in childhood is likely to be followed by subclinical infection whereas in adult life the clinical attack rate is about 50%.

"None of the 4 cases of clinical hepatitis occurring during the study were antigen positive, and this may be compared with the figure of 30-40% for post-transfusion hepatitis generally during this period."

It's undated but it's obviously written after the conclusion of the ten terms, so at some point after the summer of 1973. There's actually a more detailed interim report, I am not going to go through it in any detail, but it's at HHFT0000332.

We can see it's the same authors but it's headed "Interim Report", and if we just go to the second

page, we have a description of:

"The aim of the study ... to follow the pattern of SH (Serum Hepatitis) Antibody and antigen in boys suffering from Haemophilia and closely allied disorders resident at the College, and to see how these patterns correlated with clinical illness, frequency of transfusion and with the presence of [serum hepatitis] antigen in the blood and blood products with which they were treated."

Then it was said:

"It was hoped that some of the boys might provide serum which would be useful as a diagnostic reagent."

Whether it was known that that was being done is unclear. There's a description under the next heading of the number of boys studied, so this is in the interim stage from summer 1970 to autumn '71, at that stage 54 boys had come under observation.

Then there are findings in relation to serum hepatitis antigen and antibody.

If we go to the fifth page, there's a heading "Hepatitis". Again, I'm not going through the detail of the facts and figures but it records:

"Of the 53 boys concerned with these investigations, only 6 have a definite history of

jaundice ..."

Then reference to three of those cases contracted when at the college, the remaining three prior to entry.

Then there are various tables if we go to the next page. So there are tables in terms of showing the incidence of serum hepatitis antibody.

Next page is a table with the analysis of cases with antibody.

If we go to the next page, a table showing serum hepatitis antibody in the sera of boys suffering from coagulation disorders at Lord Mayor Treloar, and then the remaining two tables deal with patients with inhibitors and Christmas Disease.

So that's just really to give a flavour of the study. So that's one of the early hepatitis studies that was undertaken at the college.

SIR BRIAN LANGSTAFF: Can you help at all with -- if you go back to the previous document, I think it is HHFT0000053_001, and go through it, please. Next page, next page, next page, and then the next page.

What I'm looking for is there's a reference somewhere in there to there being a number of cases of post-transfusion hepatitis, not associated with the administration -- not necessarily the disease, and

I just wondered what justified it, but it's difficult to find it. But I can raise -- I'll raise it with you later.

MS RICHARDS: Yes, I'll have a look at the document again and see if there's an answer to the question, sir.

So, we see there, there's work being undertaken by Dr Rainsford in relation to studying for the incidence of hepatitis in the early part of the 1970s.

There is then further work undertaken by Dr Kirk in the mid-seventies.

If we look at CBLA0000312.

This is a document produced by Dr Kirk in September of 1975, and it is a protocol for a prospective study of hepatitis and haemophilia associated with the use of Factor VIII concentrates.

If we look at the introduction, it says:

"The transfusion of blood or its derivatives has been linked with the transmission of viral hepatitis for many years."

Then there's reference to hepatitis B, and at the end of that paragraph it says:

"This failure to prevent post transfusion hepatitis may be explained by the following hypotheses ..."

If we look at (a), (b) and (c):

"(a) That current methods of detecting [hepatitis B antigen] are still not sensitive enough."

"(b) That other known viral agents are responsible, eg, hepatitis 'A', EB virus cytomegalo virus."

"(c) That other, as yet unknown, viruses cause a significant amount of post transfusion hepatitis which is supported by the recent work of Feinstone et al."

So there is a recognition there that there is something other than hepatitis B, essentially, causing post-transfusion hepatitis.

Then if we look at the next paragraph it says:

"The introduction of large pool factor VIII concentrates into the routines management of haemophiliacs has revolutionised their treatment."

Then there are further observations made in that regard, including the introduction of home therapy.

Then halfway down that paragraph a sentence beginning:

"However, treatment with factor VIII concentrates does expose the patient to a much larger risk of contracting transfusion hepatitis since the fractionated product is processed from donor pools. Furthermore, commercial factor VIII concentrates are

made from very large pools of some 2,000-6,000 litres of plasma from paid donors. An outbreak of both non-'B' hepatitis and 'B' hepatitis associated with concentrates of this type has recently been reported by Craske et al."

There is then a reference to Prince's publication with a suggestion that:

"... recipients of all commercial blood have a ten-fold higher risk of developing non-'B' post transfusion hepatitis than recipients of all volunteer donor blood."

Then Dr Kirk says this:

"For these reasons it is proposed to conduct prospective study of hepatitis in order that the following question will be answered:

"Does the administration of factor VIII concentrates to haemophiliacs on regular replacement therapy significantly increase the incidence of transfusion hepatitis?"

So that's the purpose of the study, to look at the relationship between regular treatment with concentrates and transfusion hepatitis. Then Dr Kirk says:

"It is hoped that some additional points will emerge ...

"(a) Any difference in the attack rates between commercial factor VIII concentrates and home-produced concentrates, [namely] Oxford and Elstree.

"(b) The assessment of the value of a positive [hepatitis B antibody] test and the protection of the patient from the development of hepatitis.

"(c) Further information on hepatitis due to unknown viruses or agents other than hepatitis 'A', 'B', EB or cytomegalo virus."

Then (d) is about the role of radio immuno assay testing for hepatitis B antigen.

So it is hoped that this will provide insight into, and contribute to the knowledge of, the other causes of post-transfusion hepatitis, essentially non-A, non-B hepatitis.

We can then see reference to the method. There's reference to three centres having agreed to cooperate: Treloar's, Newcastle and Oxford Haemophilia Centre, and we've got the numbers there. We'll see what this currently envisages is 20 patients from Alton, so from Treloar's, on cryo, ten on Kryobulin, five on Elstree products. Then Newcastle will be solely Hemofil, Oxford, a mix of Hemofil and Oxford Factor VIII concentrate.

Then if we look at the text underneath that,

about halfway down that paragraph:

"Each patient will be treated with the same type of material throughout the study and where possible, batches should be arranged sequentially in order that the patient may receive the same batch of his particular brand over a period of three months. This will be difficult to achieve and the co-operation of the manufacturers has been sought in making large batches available."

So again, just pausing there, it shows an awareness of a policy of limiting exposure to hepatitis, limiting exposure to multiple donors, by adhering to one type of concentrate and, as far as possible, limiting exposure to batches of that concentrate, but this is only being contemplated for the purposes of the study rather than putting into effect as a broader approach of the treatment of all pupils at Treloar's.

We'll see that expressly acknowledged to some extent on the following page, but before we do that if we look at the "Eligibility Criteria". So:

"(a) All patients with classic haemophilia on regular replacement therapy are eligible for inclusion."

Then there's an exclusion for patients for whom

major surgical procedures are planned.

"(c) In the case of the Alton group, Lord Mayor Treloar College boys must be able to complete three academic terms ..."

(d) is a reference to preference for normal liver function at the point of entry into the study, and then (e) must be a minimum of 18 months. So:

"(e) Each patient must remain on the allotted therapeutic material for a minimum time of eighteen months. In the case of the College boys, arrangements will be made with their home centres that the allotted material is available for treatment during the vacations."

So again, it appears to be practicable to maintain a patient for the purposes of the study on the same concentrate for 18 months, but as we've observed throughout the course of the week, no attempt to achieve that, it would appear, outside the scope of the study.

SIR BRIAN LANGSTAFF: You could manage that with concentrate. You couldn't manage it quite so easily with cryoprecipitate, could you?

MS RICHARDS: In what sense, sir?

SIR BRIAN LANGSTAFF: Well, the idea of the concentrate is to stick to the same brand and the same batch. That's

possible. Because it's freeze-dried, transportable. The cryoprecipitate is made on site, generally it's not so transportable. It may simply be that cryoprecipitate of its nature comes from a limited number of donors anyway so you can never have the same batch, in effect.

MS RICHARDS: I'd read it in the latter respect, sir.

SIR BRIAN LANGSTAFF: But you'd have a different population giving rise to the plasma.

MS RICHARDS: As between the home centre and the -- and Treloar's, yes, that's correct.

SIR BRIAN LANGSTAFF: So you'd have Manchester, Newcastle, Leeds, London, cryoprecipitate finding its way through to Treloar's.

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: If anything, you'd think that would increase the chances of there being some infection in the supply.

MS RICHARDS: For those treated solely with cryoprecipitate for that period of time, perhaps, yes.

Compared to treatment -- I mean, obviously not necessarily compared to treatment with concentrates, but compared to treatment with local cryoprecipitate --

SIR BRIAN LANGSTAFF: Yes, absolutely.

MS RICHARDS: -- for an 18-month period, yes.
SIR BRIAN LANGSTAFF: It's an internal -- one sort of cryo precipitated another?
MS RICHARDS: Then the top of the next page talks about informed consent.

"All patients or their parents/guardians must give their informed consent. The following points will be made clear:

"(i) By limiting the transfused material to one type, the degree of donor exposure should be decreased."

So an express recognition there of the advantages in safety terms of limiting transfused material to one type. Then it's said that patients or parents should also be told that it will be necessary for blood samples to be taken at fortnightly intervals.

The next heading in this protocol is "Procedure". I don't need to go through the detail of that save to note that the second paragraph down refers to the taking of blood samples on a regular basis, and tested for bilirubin, SGOT, et cetera.

If we go further down -- sorry, data recording refers to data being sent to Dr Cossart at Colindale and also shared with Dr Kirk.

Then under the heading "Illness", if a patient develops symptoms suggestive of hepatitis, form C3 should be completed. That's a procedure that "should [also] be followed if the liver function tests suggest hepatitis".

Then there's a reference to the outbreak of non-B hepatitis at Treloar's the previous year, so 1974, where it's said:

"... it was found that the period of illness and abnormal liver function tests was relatively short."

Then it says:

"... should a patient become ill it will be necessary for serial blood samples to be taken for LFTs - perhaps twice weekly, depending on the clinical status of the patient."

Bottom of the page refers to arrangements during the holidays:

"Lord Mayor Treloar College boys require special arrangements for their treatment during the Christmas, Easter and Summer vacations to ensure continuity of therapy. College boys on concentrates have been selected from the following centres only - Oxford, The Royal Free and Newcastle. Arrangements are being made with these Centres that the boys receive only the therapeutic material to which they have been allotted.

Those boys on cryoprecipitate have been selected from treatment centres where only this material is available."

Then if we go to the third paragraph on that page:

"Commercial manufacturers, viz Travenol Laboratories and Serological Products have agreed to reserve large batches of concentrates for this study. The Directors, or their deputies, will be responsible for ensuring that a patient receives only his allotted material for a period of eighteen months after entry. Batches should be arranged so that an individual receives preferably only one batch over a three-month period."

Then there are references to testing analysis, possible future extension of the study. It's said it is proposed to acquaint the UK Haemophilia Centre Directors with the pilot study at the meeting in September 1975 and those are the minutes of the meeting we looked at before lunch.

Then bottom of the page:

"Although this is, in principle, a simple study the operation and organisation of batches of material will present some problems. However, the actual units of factor VIII used will be no greater than in the

normal day to day treatment and the study may indeed be viewed as a rationalisation of replacement therapy, since the probable donor exposure to each participant should be less than that experienced prior to his entry to this study."

So it's essentially being said that this -- I'm paraphrasing, clearly, but this is a benign thing for participants because their donor exposure is going to be reduced. What it doesn't explain is why, if that's the understanding, that's not the broad approach to therapy at Treloar's in any event.

So that's the protocol produced by Dr Kirk in September 1975. As I say, I won't go back to the discussion that was then held a few days later at the Haemophilia Centre Directors meeting about the study. There's a subsequent document which I'm going to go to later so I won't go to it now, but what it shows in fact in relation to Treloar's boys, 21 boys restricted to cryoprecipitate for the study, eight Kryobulin, six Hemofil, one Profilate, four given Elstree concentrate, and five Factor IX.

There is some evidence of consent being sought, interaction with the parents, and so, although it's not clear what information is then -- has been provided to elicit the consent, but we've just got

a handful of examples of documents.

If we look first of all at TREL0000225_048, we can see a letter from Dr Kirk, December 1975. We looked I think at a very similar letter earlier in the week saying:

"In view of the problems of hepatitis in haemophilia, I have been asked by Dr Rosemary Biggs, of the Oxford Haemophilia Centre, to conduct a survey on this subject."

Whether that's -- assuming this relates to the same study, whether that's an entirely accurate way of describing a study set up and authored by Dr Kirk is -- it may be questionable.

"Your son has been selected to receive only cryo when he requires transfusing. By limiting him to this type of factor VIII containing material it will be easier to trace the source should he contract hepatitis.

"If you have any queries concerning this survey I would be happy to discuss the matter with you."

So that appears to be the information that was provided, at least on this occasion, to a parent. It looks like it's a fairly standard form document, it's "Dear" and then blank.

Then there is some correspondence which shows

that she's given him Kryobulin, and saying in the last paragraph:

"I am sorry in this will interfere with your hepatitis trial."

So again, obviously, knowledge from the home haemophilia clinician of the trial but doesn't tell us what was known by the patient or pupil.

If we go to TREL0000103_018, we've got a letter here from April 1976 from Dr Kirk to a Dr Peard in Horsham, again referring to a particular pupil:

"As you know, this boy is on the hepatitis study and I have just received the results of his liver function tests.

"He would appear to be developing hepatitis which is probably associated with an infusion of Factor VIII concentrate (Hemofil B) on 15 February 1976."

Then reference is made to hepatitis B being negative, so it is possible that he's developing hepatitis maybe of the B or non-B type:

"Please could you let me know if he becomes ill and should you see him I would appreciate further blood samples. If he requires admission I would be pleased to come to Horsham and see him."

There doesn't appear to be any suggestion there

discussions between Dr Kirk and the home Haemophilia Centre in relation to this study, so we can again look at some examples.

TREL0000280_074.

This is Dr Mann at Birmingham Children's Hospital to Dr Kirk in September 1975, second paragraph:

"We would be pleased to help in your study ... do in fact only use cryoprecipitate for our haemophiliacs, with one or two rare exceptions ..."

And then refers to two patients and then says, last paragraph:

"Please could you let me know when you wish to start this study? The quantities of blood which you will be removing will be quite large, and I wonder whether you had thought of giving iron therapy too?"

Is the question posed.

So there's an interaction with the home haemophilia clinician but doesn't tell us what, if anything, has been said to the patient or the patient's parents, in that regard.

TREL0000211_022 is a little later on, April '77, but we can see from the last sentence it is concerned with the hepatitis trial. This is from Dr Swinburne to Dr Kirk in relation to a particular patient saying

of a change of course or a change of therapy, it's just an identification that through the concentrate being provided to this patient on the study, that they appear to be in the process of developing hepatitis.

Then if we go to OXUH0003758_006.

This is one of the reports produced by Dr Kirk. This is date 20 April 1976, and it's a report on the autumn term '75 and spring term '76 and there's a discussion of the hepatitis study on page 5. It says:

"This started at the beginning of the Autumn term and the conditions for entry and other requirements are recorded elsewhere in the Protocol."

So this appears to pre-date some of the other documents, this is suggesting that the start of the study may have predated, I think, some of the other documents we've looked at. But in any event:

"The boys were restricted to a particular type of factor VIII replacement material. This is shown in Table VI.

"Seventeen cases from Oxford ... were included from November 1975 whilst two Edinburgh patients joined in February 1976. It is apparent that in conducting a survey of this type it is difficult to ensure the collection of frequent blood samples unless

the patients are readily available. Furthermore, limiting patients to particular replacement materials also creates problems because of the overall shortage of factor VIII products. It is inevitable that some patients will receive, and have received, materials other than their specified product. The nursing and laboratory staff are to be congratulated on the careful and thorough way that specimens have been collected, separated and dispatched to the Virus Reference Laboratory. The work of Dr Hugh Platt and the Chemical Pathology Department of Basingstoke District Hospital has been invaluable in processing large numbers of liver function tests which has been accomplished quickly and efficiently".

Then if we go further down it says:

"So far no patients from Newcastle have registered on the study but it is hoped that 12 patients restricted to Hemofil will be included in the near future."

Then this:

"Since the start, three of the College boys have contracted hepatitis."

Details are then given. The first is a boy who was restricted to Kryobulin. The last sentence of that paragraph says:

"Provisionally he has been labelled as a case of anicteric non-B hepatitis."

The second boy is described as showing clinical and laboratory evidence of hepatitis soon after being entered on the hepatitis study. It says at the bottom of the page:

"This case is interesting in that the probable source of the infective material can be identified ..."

And again the reference is to particular batches of Kryobulin:

"This was his first exposure to large pool concentrates ..."

Then the third is a patient described as a mild haemophiliac, which doesn't fit with what else we know about pupils at the college but, in any event, it refers to that patient receiving Hemofil. Said to be at risk of developing hepatitis B, and is going to be investigated further in the summer term.

Then the next paragraph:

"Apart from these three cases of acute hepatitis, a number of boys have permanently elevated liver function tests. At present work is directed at determining the significance of these findings for it is important to ascertain whether they are suffering

from chronic hepatitis and, if they are, whether this is benign or an aggressive process. Four boys have had liver scans which all show mild, but very definite, abnormalities. It is proposed to do further scans next term on other indicated boys. Regarding the problem with the acute hepatitis cases, it is important to exclude other causes of hepatitis apart from hepatitis B, namely: hepatitis A, cytomegalovirus and EB virus."

Then there's a reference to hepatitis A.

Sir, I think you asked earlier in the week about tests for hepatitis A. This tells us that a suitable test has not yet been devised which is uniformly satisfactory in relation --

SIR BRIAN LANGSTAFF: No, part of what lay behind the question was a sense that non-A, non-B has plainly been identified in some of the studies since 1974, if not before.

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: And that suggests that A can be excluded, so there has to be some basis for excluding it.

MS RICHARDS: Yes.

SIR BRIAN LANGSTAFF: And I had assumed, without actually knowing it, that there was therefore a test. This

looks as though there is a test, although it is not a very good one.

MS RICHARDS: That seems to be Dr Kirk's view.

Then it continues with a discussion about the arrangements for the testing of samples.

And then -- sorry, that's the discussion, then, in this report about the hepatitis study, so we can see as at April 1976 it's identifying three boys with hepatitis and number of boys with permanently elevated liver function tests.

If we just finish by going to the next page, just below the heading "Home Treatment", so the next paragraph down, I just draw attention to this, it's not specifically relating to research as I understand it, but it says:

"Finally, acknowledgement must be made to the Army Blood Supply Depot at Aldershot, under the direction of Colonel John Winwick, for their continued help both in the supply of therapeutic materials in an emergency and the provision of normal plasma for use as standards in the variety of coagulation tests performed at this Centre."

So it would appear in some respect or another the Army Blood Supply Depot is providing materials to Treloar's.

If we can then go to page 11, I referred earlier to who was getting what on the hepatitis study. You can see here where the figures that I referred to were drawn from, so cryoprecipitate, Kryobulin, Hemofil, Profilate, Lister, Elstree concentrate and then Factor IX.

There are, again, a handful of further documents relating to information being provided to parents and/or clinicians about participation in the study.

So TREL0000064_017 is a sheet of some kind about a particular patient, saying:

"The above named patient is involved in a national prospective hepatitis study. It is thus very important that he receives only f.VIII containing material of one type: in his case: CRYOPRECIPITATE."

So he's one of the category of boys receiving cryoprecipitate, and that's signed by Dr Kirk.

Then TREL0000250_016 is a letter, September 1975. So, again, it demonstrates that there are communications ongoing between Dr Kirk in relation to the hepatitis study and other clinicians, but less clear as to the extent of parental or patient involvement.

"Dear Dr Kirk,

"Thank you for your letter concerning your

differences between the cases restricted to Hemofil and Kryobulin. In the next stage of the Study, I am proposing to restrict patients to either commercial concentrates as a group or Cryoprecipitate or Lister Concentrate as I understand that all commercial Factor VIII concentrates are being made from North American plasma, including Kryobulin."

So that issue again about the source of Kryobulin donations is there addressed.

"Would you have any objections to these proposals or do you think it would still be worthwhile to restrict patients to a particular brand of commercial Factor VIII concentrate?"

There's an update of the position as of April 1977.

Then in October 1977, there's a letter from Dr Craske to Dr Aronstam at HHFT0000925_001, 7 October 1977.

First paragraph refers to:

"The arrangement which I had with Peter Kirk is that we had been testing bloods taken from the boys at intervals over the past two years as part of the prospective study of the incidence of hepatitis, and abnormal liver function tests associated with different forms of Factor VIII therapy. Peter Kirk is

proposed study of patients with haemophilia.

"In answer to your queries:

"1. We will certainly find it easy to give [the patient] cryoprecipitate only when he needs treatment.

"2. The blood samples that you require. We will certainly collect clotted blood samples whenever he has treatment."

Then the same question as Dr Mann had posed:

"Are you going to put the children on prophylactic iron therapy?!"

Then 3:

"I would be pleased to notify you if [he] would develop hepatitis."

Again, that doesn't tell us anything about what the pupil or parents knew.

Then CBLA0000590. It's an update from Dr Kirk on 1 April 1977 to Dr McGrath at the National Institute for Biological Standards.

"Dear David,

"We have been conducting the Hepatitis Survey for some 19 months and are almost in a position to have a significant result. All the cases of clinical hepatitis and almost all the cases of asymptomatic hepatitis were confined to the patients restricted to commercial concentrates. There were no significant

now writing up his results."

Just pausing there, there doesn't appear to be any positive evidence of pupils or patients being aware of bloods being tested in this way.

Then Dr Craske says:

"I [am] keen to continue our collaboration; this is for two reasons:-

"1) We are interested in doing more work to try and establish the aetiology of the non-B hepatitis we have found associated particularly with commercial freeze-dried Factor VIII [concentrates].

"2) I think it will be valuables to take serial serum samples from these boys with the idea of trying new tests, particularly those thought to give good correlation with chronic liver damage."

Then picking that up in not the next paragraph but the one below:

"We are particularly keen to obtain specimens as early as possible from patients in whom hepatitis is suspected ..."

Then the last sentence of that paragraph:

"In the absence of any symptoms of disease I would suggest taking a blood specimen once a term from each boy, this will give us pre-infection sera should any hepatitis become evident at a later date."

So it would appear a bank to stored samples essentially being built up there from Treloar's pupils, with those samples being sent to the Public Health Laboratory Service under Dr Craske.

Just actually on a separate point, but if we look at the last paragraph, Dr Craske says:

"I shall be at the annual meeting of Haemophilia Centre Directors at Oxford on the 24th October ... if you wish, we can talk about this further on that occasion."

Of course it is important to bear in mind that whilst we have the minutes of the various Haemophilia Centre Directors meetings, what they won't capture are all the kinds of exchanges and discussions that might have gone on outside a formal setting during the Haemophilia Centre Directors meetings.

Then I think there's just two more documents in relation to the hepatitis study.

The first is at HCDO0000544.

This is one set of minutes from the Hepatitis Working Party. The date is 14 December 1977, and Dr Kirk was a member of the Hepatitis Working Party. Under the heading, "Investigation of Chronic Hepatitis - Indication for Liver Biopsy", the minutes record as follows:

"Dr. Kirk opened the discussion by describing the results of the prospective survey on hepatitis carried out at Edinburgh and Alton. Forty-five boys at Alton aged between 11 and 16 had been studied. There was a higher proportion of patients treated with freeze-dried products who had consistently abnormal liver enzyme tests, compared with the boys treated with cryoprecipitate. Fifteen of these boys had a SGOT of at least two and a half times the upper limit of normal for most of the period studied. They were well and had no clinical evidence of chronic liver disease."

Then there's reference to palpability of the spleen and liver being enlarged in some cases:

"Five ... boys ... found to have abnormal BSP tests ... no definite correlation with previous Factor VII therapy, though this had yet to be fully investigated."

In the next paragraph Dr Kirk continues:

"... two other boys with clinical symptoms and signs consistent with chronic active hepatitis. One had hepatitis B after a transfusion of Hemofil in 1974. He has evidence of chronic liver disease and is still HB Ag positive three years after his acute attack. The second patient had normal LFT's prior to

an acute attack of Hemofil associated non-B hepatitis. He still has abnormal liver function tests."

There is then recorded a discussion of problems associated with the interpretation of abnormal liver function tests and liver disease in haemophiliacs.

Then there's a further discussion over the page, I won't go through the detail of it because it goes wider now than the question of the hepatitis studies at Treloar's, but there's a discussion about liver biopsy, discussion about investigation of liver disease, and three categories identified of patients with abnormal liver function tests, and then a proposal for investigations and recommendations to the Haemophilia Centre Directors.

The last document then is an application for a research grant from Dr Craske, so it's not directly from Treloar's, but it does involve or include some information about Treloar's.

CBLA0000756. It's a letter from a Mr or Ms Buxton, principal medical officer to Dr Maycock, 19 April 1978, and you'll see it refers to an attached application for a research grant from Dr Craske.

If we go to page 6 we can see Dr Craske is there recording under the heading -- bottom of the page, I'm sorry:

"Chronic sequelae

"A recent study carried by members of the Haemophilia Directors' Hepatitis Working Party, in which groups of haemophiliacs were confined to one type of Factor VIII treatment, as far as possible, has shown that 15/45 boys at the Lord Mayor Treloar College, Alton, had consistently elevated serum enzyme levels (two and a half times the upper limit of normal) for periods of six months or more. There was a due association with the use of freeze dried Factor VIII concentrate", et cetera, et cetera, reference to having evidence of chronic active hepatitis, one hepatitis B.

Then the question Dr Craske poses in the next paragraph is:

"... whether these changes are indicative of early liver disease which, in a proportion of patients, may be the forerunner of chronic active hepatitis or cirrhosis."

Then a reference to non-A, non-B hepatitis.

Those are probably the most salient documents relating to the hepatitis studies at Treloar's, but it is clear that the incidence of hepatitis in boys at Treloar's was studied over a prolonged period of time in the 1970s, with then this particular focus under

Dr Kirk on limiting treatment to one type of product add then examining the consequences, and we've seen some of the results that were then reported.

I should say what we don't see is any indication of any change in therapy or change in the approach to treatment following the hepatitis studies.

Before I move on to look much more shortly at a handful of the other types of research that are undertaken at Treloar's, there's just one document which takes me back to the prophylactic studies and the question of what information was or wasn't made available to parents or patients.

Soumik, could we have -- and this will have been sent to you this afternoon, I think, CGRA0001060. Thank you. You are ahead of me.

It's a letter from Dr Jones Newcastle, dated 12 April 1973.

"Dear Mr and Mrs Longstaff.

"I am sorry that you could not come to the last clinic and I enclose another appointment. You will have received a letter from Lord Mayor Treloar asking for your permission for Peter to participate in the special trial of regular factor VIII injections."

So that suggests there was a letter directly from Treloar's to parents at least in this case.

Refers to someone else's parents also being accounts for their permission. Then we can see Dr Jones saying this:

"I saw the [reference to other set of parents] last week and explained that I was in complete agreement with the trial and that it could do nothing but good for the boys and for other patients. It has been most carefully worked out, was discussed at the last meeting of the Haemophilia Directors in Oxford, and has the support of the Medical Research Council of the United Kingdom. I will of course be extremely happy to discuss any points that concern you about the trial when I see you, but I wonder if you would feel able to sign the acceptance form for Lord Mayor Treloar at this stage."

It refers to doctors trying to get things organised for the next term.

Now this because of the date and because of the reference to the involvement of the Medical Research Council must be a reference to the first trial of prophylaxis, which of course involved placebos. And you'll see, sir, there's no reference at least in this material, and indeed Dr Jones's approval of the trial saying it could do nothing but good for the boys and other patients, there's no reference there to the

receipt or use of placebo.

Just then going to, as I say, deal very much more shortly with a handful of other types of research that we know were undertaken at Treloar's.

So if we look at RLIT0000198, on the right-hand side, and this a publication in the Lancet in 1980. There's a heading:

"Double-blind controlled trial of three dosage regimens in the treatment of haemarthroses in haemophilia A."

And this was one of I think we've said in our written note three studies but I think it is probably in fact two studies, three reports referring to actual studies, conduct at Treloar's to investigate the optimum dosage of Factor VIII required to treat a bleed. As I say, I won't go into the detail of it but we can see here reference to the double-blind controlled trial in terms of three dosage regime. That's written up in 1980.

And then there's a further publication at RLIT0000098.

This is probably about the same underlying study, but there is a second double-blind controlled trial at RLIT0000111.

And we can see this is "... a double-blind

controlled trial of two dose levels of factor VIII in the treatment of high risk haemarthroses in haemophilia A". Again, I'm not going to go through the detail of them but it is a further evidence of a different type of research being undertaken, and trials being undertaken in relation to the pupils at Treloar's. I just want to then look at a handful of documents that show a degree of interaction with parents, some in relation to this, the double blind controlled trials of three or two doses, and some may be in relation to other aspects of research or trials at Treloar's.

But it gives us a flavour of some of the interaction between Treloar's and parents.

TREL0000105_040.

So this is a letter from a parent May 1978 to Dr Aronstam and Dr Painter.

"Thank you for your recent letter concerning the higher dosage of Factor VIII. Whilst I agree to the first part of your programme (the higher dosage) I do not feel I can give my permission to your other suggestion concerning the other substance you mention. Before agreeing to anything like this I would like to know a lot more about this 'other substance', and for it to be tested at length so I would ask you not to

include [then the patient name redacted] in your programme."

So there has clearly been a form of correspondence from Treloar's directly to a parent in relation to what appears to be the trial relating to higher dosages, but perhaps an indication of a lack of sufficient information to enable the parent to feel comfortable giving consent to all aspects of what had been required.

Again, there is a letter expressing similar concerns from a different parent at TREL0000147_018.

A letter in fact of the same date, this addressed to Dr Painter, suggesting agreement that the patient "should take part in your first project". So again, there's a letter referring to two projects.

"If the second project only requires the monitoring of one bleed then this also has our consent. As a matter of interest we would be grateful if you would let us know the nature of the 'other substance' and the results you would hope to obtain."

So again, some indication that whatever letter has gone out to parents from Treloar's, it's not giving information about what the actual substance is, that it's proposed the pupils should be treated with.

Then again, the same month, TREL0000070_027,

there's a letter from another parent, which says:

"We agree that if [some] definitive information can be obtained on the dosages of Factor VIII required that would be helpful. However, we are not happy about our son ... being included in an investigation conducted as you describe. We are anxious that the total amount of Factor VIII he receives should be kept to a minimum, particularly to lessen the risk of his developing antibodies to the material. Over recent holidays we have found that for most bleeds if they are treated promptly, and with sensible behaviour on [his] part, 3 240-unit bottles of Hemofil are sufficient to arrest the bleeding and avoid a recurrence. For a bleed in a 'difficult' place or if treatment is delayed a larger dose is necessary and the risk of a recurrence is considerable. From what we learn from [the pupil], it seems to me that the dose he normally receives at the Treloar Haemophilia Centre is quite high and we would not wish him to receive a higher dose except in [particular] circumstances."

SIR BRIAN LANGSTAFF: "Peculiar circumstances".

MS RICHARDS: "... except in peculiar circumstances."

Sorry.

"As regards [his] participation in a study of

the effects of a substance [again undefined what that is] which might improve the efficacy of the Factor VIII given, we would have no objection - in fact we are enthusiastic about him doing so."

There a patient -- a parent expressing particular concerns. Again, it gives rise to the question and unfortunately we don't have copies of all the correspondence that went out from Treloar's, although we may still locate it. But it raises the question of whether the implications of receiving higher dosages, possible increased risks, had been spelt out to all parents. This is a parent who seems to be reaching that conclusion as it were on their own initiative or based on their own knowledge.

There is then, at TREL0000147_019, a reply from Dr Painter to one of the letters which indicates what the other substance is, or provides some other information about the other substance. We're told that:

"... it is in fact a hormone produced in the body and has the effect of concentrating the urine whenever the intake of blood is reduced ... has been found to raise the Factor VIII level in mild haemophiliacs ... As far as we can ascertain, no-one has tried the effects of using this substance in

conjunction with a transfusion of Factor VIII in a severe haemophiliac [and so] we intend to try this to see if it might either prolong the effective life of the injected material or perhaps enable a smaller dose to be as effective over a given period of time as the larger one."

So we see the explanation there but it perhaps begs the question of why the explanation was not included in the information that was provided to parents in the first instance. The details of who this letter is addressed to is redacted, but what I can say, and it's interesting to note, is this is actually a letter addressed to a doctor who it appears may also have been a parent. And so an informed parent may have been able to raise questions and get an answer, and get information which should perhaps have been included in whatever is provided to parents in the first instance.

There are then, I'm not going to go to them, I think but there are then again a handful of communications between Treloar's and doctors who are treating haemophilia clinicians about involvement in these studies.

Perhaps one worth looking at TREL0000327_005.

Here we have Dr Aronstam writing to

Dr Swinburne. The first paragraph refers to the trial comparing a normal with a high dose for bleeds, and he says:

"I enclose a copy of a paper based on the identification of the high risk bleeds for your information."

So again, we can see information being provided to treating haemophilia clinicians but it's not apparent that the same information is being provided to parents.

Then a further type of research that was undertaken at Treloar's is apparent from HHFT0001201_004, and so this is an outline protocol produced by Dr Jones and Dr Aronstam, and we can see the aim describes the study as:

"... [forming] Stage I of a proposed investigation into the potential benefits of High Purity Factorate. The results obtained will form the basis of the decision to proceed to Stage II - a trial of Factorate in the prophylactic management of Haemophilia."

Then:

"The objective ... is to compare the in-vivo half-life and recovery of High Purity Factorate with that of another commercially available factor VIII

concentrate of Intermediate Purity (Hemofil No. 2)"

A little further down the page, under the heading "Patient Numbers", it says there's a minimum number of 12:

"Two centres will participate, with a minimum number at each centre of 6."

The bottom of the page tells us that the products to be used are Armour, Factorate High Purity and Hemofil produced by Travenol.

If we go over the page, we can see the dose is to be calculated so that the patient's Factor VIII level will be raised to 50%.

There's then reference to investigations in a range of blood samples. It says:

"The samples will be treated as fresh specimens at each Centre."

But someone has then written "+ stored!"

Then the bottom of the page refers under the heading "Ethics":

"Informed consent will be obtained from all patients, who will have the right to refuse or to withdraw consent without prejudice to their routine treatment.

"The investigators undertake this pilot study on their own responsibility and do not need the agreement

of an Ethical Committee. There is no Regulatory implication in this study."

Again, what we don't have is any kind of understanding of the information being provided to patients or parents to elicit informed consent.

If we go to TREL0000012_113, we can see here a document we've seen now on a number of occasions, so the consent form which gives no information about what trial is being consented to. It's just says "a trial ... as explained by Dr Aronstam".

The reason for referring to it is if we go over the page, we've got a very slightly different form, where here the agreement is to:

"... taking part in the trial of a new Factor VIII product as explained by Dr Aronstam."

It still doesn't say what the product is. But somebody has written on the top, "HL [half life] Trial", which would tend to suggest that it may be related to the protocol that we just looked at.

And again, if we look at TREL0000108_158, we've got another example of a consent form in this format. So again, someone has handwritten on it "HL [half life] trial", and the consent is to taking part in a new Factor VIII product as explained by Dr Aronstam.

There are some comments from the bottom of the

page from the parents saying:

"... very pleased to hear a new type of Factor VIII has been manufactured and only hope it proves successful."

Again, we can't ascertain from this what information has actually been provided to the patient, or their parents.

This work was written up at RLIT0000104.

I'm not proposing to go through the details of it. We can see it was written up by a number of authors and it refers to the involvement of both Treloar's and the Royal Victoria Infirmary at Newcastle upon Tyne. It may just be interesting to note at page 6, under the heading "Acknowledgments":

"This work was supported by a grant from Armour Pharmaceutical Company Ltd."

If we go to HHFT0001201_003, we can see a letter from Armour to Dr Jones dated 23 December 1980, and it would appear from this that Armour have had some considerable involvement in the development of the protocol and it refers to a discussion in Alton, so presumably at Treloar's.

"Please find enclosed a copy of a Protocol, revised according to our discussion in Alton on 1st December."

And then it refers then to discussion and agreement about various points:

"The ... centres taking part will be Newcastle and Alton.

"... each centre will recruit a minimum number of 6 cases ...

"The study will start in January 1981."

There's then an estimate of costs.

If we go over the page, agreement that the costs will be met from research funds initially, and then Armour are going to reimburse on receipt of an invoice.

"We agreed that the Hemofil 2 would be obtained and provided by us. We therefore need to know as a matter of urgency the quantities which you and Dr Aronstam calculate to be necessary."

So a degree of close involvement it would appear from Armour in that trial which obviously was seeking to compare an Armour product with the Hemofil product.

Then there are just, I think, just a few examples of other forms of treatment that I can refer to. I think probably in about 10 or 15 minutes so it may be worth completing it rather than having a break and coming back, if --

SIR BRIAN LANGSTAFF: Yes, well, let's do that then, shall

we. But if you begin to think that it's going to take too long --

MS RICHARDS: Yes, I will --

SIR BRIAN LANGSTAFF: Do remember people might appreciate a break.

MS RICHARDS: Yes.

So another area of study was trials of Autoplex. The report of that is at RLIT0000110. I think I can just refer to the heading here:

"The use of an activated factor IX complex (Autoplex) and the management of haemarthroses in haemophiliacs with antibodies to factor VIII."

We can see there again, it's origin is Treloar Haemophilia Centre.

So that's a study resulting in this publication, a study I think carried out probably in 1980, 1981, published in 1982. There was a further study under the auspices of the UKHCDO's Inhibitor Working Party. It may be worth just looking at that.

It's OXUH0000447_002.

Sir, this is a report of the UK Factor VIII Inhibitor Working Party in October '83, so a subsequent study continuing the trial of Autoplex versus Factor VIII. Again, I am not proposing to go through the detail of it but if we go to the second

page, we can see in paragraph 3:

"Concern has been expressed as to whether AIDS might be introduced into U.K. haemophiliacs via the use of Hyland factor VIII or Autoplex. The Chairman of the Working Party has sought clarification from Travenol Laboratories as to whether any of their material is known to have produced this problem in the United States and it is hoped that an answer to this question will be available at the meeting."

There is also, in relation to the UKHCDO study, some evidence of patient information, HHFT0001161. Sir, this not the solely Treloar's study, this is the UKHCDO's Inhibitor Working Party study, but we can see it's headed "Patient Consent Form", and this appears possibly to be a draft of some form of patient information leaflet.

If we go to the third page you'll see that there is then a consent form, a blank standard consent form.

But there is no evidence which indicates what form of consent, if any, was sought for the first Autoplex trial undertaken under the auspices of Treloar's alone in 1980 and 1981.

We know there was also a study in relation to DDAVP. There is again some evidence of exchanges between Treloar's and parents in relation to that.

Although the information is relatively limited and there's no patient information leaflet or anything of that kind.

If we look at HHFT0001430, we've got some handwritten notes about the involvement of seven Treloar's patients in a DDAVP trial in the summer of 1982.

That was published at RLIT0000124, and I think also we can see:

"The Influence of DDAVP on the Survival of Factor VIII in Severe Haemophiliacs."

McLellan, Knight, McLellan, Wassef, Aronstam, Treloar Haemophilia Centre.

Again, I'm not going to go to the detail, this is really just to try to give an understanding of the very wide range of research work and trials that were undertaken at Treloar's.

There is also evidence of a number of students with inhibitors trialing the tolerance inducing protocol, and we saw reference to that with one of the witnesses earlier this week. We've got a number of examples of individual patients, individual pupils, being involved in that process. I won't go through the detail of them because they don't greatly add to the oral evidence you've already heard about that.

The one letter that may be worth looking at is a rather later one in time, HHFT0000145_002. Just before I look at this, the trials in relation to the tolerance-inducing protocols for patients with inhibitors in Treloar's appear to have been taking place in the early part of the 1980s. It's perhaps interesting to note in this letter in 1993 from Dr Wassef to Dr Wallsley(?) at Poole, looking at the paragraph beginning, "With regard to", the third sentence reads:

"Inducing protocols [tolerance inducing] are now coming to the fore again as treaters are encouraged by the safety of materials."

So it tends to suggest that they, as it were, perhaps unsurprisingly, fell out of popularity with clinicians because of safety concerns and there is now consideration being given to the reintroduction of them.

There's one of the documents -- there is a document in which Dr Wassef -- sorry, Dr Aronstam expresses a concern about the use of the level of use of Factor VIII exposure but I don't think I have a reference to that it may be one of the documents we looked at this morning.

SIR BRIAN LANGSTAFF: You give it -- I think it's in the

fact of a parent refusing to give their consent, and indicating that at the bottom of the form.

Sir, there are just two further documents, then, I want to look at today and they're just indications of some of the interactions between Treloar's and pharmaceutical representatives. So we've seen some indication of that already.

IPSN0000331_001 is a letter from Speywood to Dr Aronstam July 1980 and it's, I think, just one of a range of communications from Speywood we've seen in relation to different Haemophilia Centre Directors at the time, but it's an approach to Dr Aronstam talking about porcine product, in the second paragraph, and making that available. Referring to difficulties in terms of financing the research, and then offering savings, towards the bottom of the page, on the price of Humanate. Offering administration kits free of charge, offering delivery within 24 hours, and so on. Top of the next page, Mr Williams, the director says:

"I do hope you will be able to give us some support and use Humanate for part of your treatment programme."

We don't have any particular response from Dr Aronstam to that letter so that might be thought to be a fairly typical approach from what we've seen in

study, TREL0000173_070.

MS RICHARDS: I'm not sure that's the right reference, I'm afraid, and I don't seem to have my hard copy. Yes, I think we may have looked at this with one of the witnesses in fact. If we look down the bottom of the page -- yes, it is that paragraph. Thank you, sir.

It's the paragraph beginning:

"We have given him enough material to continue his protocol through the summer ... We did try increasing his exposure to antigen [et cetera, et cetera]. It is possibly wrong to continue his exposure to factor VIII at this level and I would be interested in your own opinion."

The timing of this letter is July '83, so it's not clear precisely what Dr Aronstam has in mind in writing that, but in a letter from Aronstam to Professor Bloom in July '83 might suggest that the underlying concern to which Dr Aronstam was giving limited voice is about the risk of AIDS.

Again, we've various examples of consent forms, very much along the lines of the amongst we've already looked at, they simply don't explain in the form what it is the parent is consenting to so we've got multiple other examples, all undated, along the lines we've already looked at. We've got one example in

relation to other centres from a pharmaceutical company to a Centre Director.

Then if we go to BAYP0000021_063, this is an internal board meeting of Cutter Laboratories, December 1980. The relevance for present purposes is what's said at page 5, paragraph 8:

"It was agreed that full investigation should go into the promises made by Carroll Jones and Sidney Pugh to the Alton Centre where Doctor Aronstam had been promised some form of financial support for a research fellowship and had put in a great deal of time and effort in putting forward a representation to the Company. However, nothing materialised and it seems that this was causing the Alton Centre to have nothing to do with Cutter whatsoever. It was agreed that this should now be looked into again with a view to the Company being in a position to offer some form of financial support for such a fellowship."

We don't presently have any more information about this particular issue. But it does appear to indicate perhaps a relationship between that which a pharmaceutical company does or does not make available to Dr Aronstam at Treloar's, and Dr Aronstam's decisions about what products to purchase for the Centre.

Sir, those are the documentary materials in relation to research that I wanted to draw to the attention of those listening and to you. There are obviously other documents as well, but we hope that gives some indication of the breadth and scope of research that was being undertaken at Treloar's, really from the late 60s, 1970 onwards. throughout the 1970s and well into the 1980s.

In terms of the question of the significance of this research activity more generally, there may be three issues which arise, and I'll identify them now because I've no doubt that they are matters upon which participants may wish to make submissions in due course.

There's first of all the issue of patient consent, and whether the ethical guidelines and requirements in relation to obtaining informed patient consent were adhered to and we've seen, obviously, a range of material in that respect, and indeed, in relation to a number of the studies, a dearth of material.

The second broad issue, the ethical implications of the particular study or trial or research and the ethical implications of an individual pupil's involvement in that research or trial, in other words,

were there aspects of that particular piece of research, that particular study, which might have led to the pupil being treated for their haemophilia in a less than desirable or in an unsafe fashion, or in a way that's increased the risk of exposure to viral infection?

So that's looking at things essentially on a trial-by-trial, piece-of-research by piece-of-research basis.

Then the third issue is really to stand back and look at the bigger picture of a pattern of research, a pattern of studies, over many years in Treloar's, and ask whether the focus on studying what is repeatedly referred to as this unique group who offer unique opportunities for clinical and laboratory observation, whether that focus may have contributed to a mindset on the part of the clinicians involved with the care of pupils at Treloar's in which they may have lost sight of questions about how properly to treat individuals, how properly to communicate with individuals as patients, and whether there was a mindset of seeing pupils as objects for research and study foremost, rather than as individual patients first and foremost.

Sir, I raise those as issues that you may want

to consider in due course, and that others may want to make submissions on in due course. There may be a multiplicity of other issues that arise out of the examination of the research undertaken at Treloar's.

SIR BRIAN LANGSTAFF: Well, presumably your second includes not only the ethical implications of inclusion in a study, but of exclusion from it?

MS RICHARDS: Yes. Yes, so if we take the Hepatitis Survey and limiting patients to one concentrate, which might be thought to be a better thing than the ordinary treatment regime, the patients who are not being included on it are, by definition, continuing to be exposed to multiple concentrates.

SIR BRIAN LANGSTAFF: Because I can see there may be an argument that the rationale for doing the study would suggest that that should be the norm, as opposed to the exception. But that's a matter for submission in due course.

MS RICHARDS: Indeed.

Sir, that completes the review of the documentary material for the purposes of this week's hearings.

SIR BRIAN LANGSTAFF: Yes. Well, that concludes this presentation, does it?

MS RICHARDS: It does, sir.

I should say that the written note which refers to many -- not all of the documents, but most of the documents that I've drawn attention to in the week, will be published on the Inquiry's website, probably next week, which will enable all those interested to view it. It's already obviously been made available to legal representatives and Core Participants, but it will enable everyone who wishes to, to see what it says.

SIR BRIAN LANGSTAFF: And looking ahead beyond next week?

MS RICHARDS: We have a break in hearings, not a break in work, but a break in hearings for three weeks, and then we resume on I think it's 19 July.

SIR BRIAN LANGSTAFF: I think it is too.

MS RICHARDS: Is that correct? For what will be a busy two weeks. We are anticipating hearing three days of evidence from Dr Diana Walford, medical officer within the Department of Health, and then two days' of evidence from Lord Simon Glenarthur, minister in key parts in the 1980s.

SIR BRIAN LANGSTAFF: And that's the week beginning the 19th?

MS RICHARDS: That's the week beginning the 19th, so we're anticipating sitting for five days that week.

Then in the following week, so the week

beginning the 26th, we're sitting, we hope, on the 27th, 28th and 29th to hear the evidence of Lord Kenneth Clarke.

SIR BRIAN LANGSTAFF: Thank you. So 19 July, ten o'clock.

MS RICHARDS: Thank you, sir.

(3.25 pm)

(Adjourned until 19 July 2021 at 10.00 am)

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