Friday, 11 March 2011

(9.30 am)

MS DUNLOP: Good morning, sir. Today we are looking at the circumstances of the fourth person who we are asked to consider. We are looking at Alexander Laing, who was born on 7 December 1923 and who died on 4 September 2003.

THE CHAIRMAN: This is the last of the remaining deaths in the term of reference?

MS DUNLOP: This is the last of the deaths in the term of reference, yes.

THE CHAIRMAN: I don't know if the ladies and gentlemen who are attending will necessarily know that the terms of reference were changed so as to delete one of the original cases but that explains why we are dealing with four only.

MS DUNLOP: Sir, in common with Mrs Black, Mrs Laing is rather frail and I think would have found it too much of an ordeal to come here and give evidence. But we do have her statement and I should ask for that to be displayed on the screen now, please. It is [WIT0030417].

If we look at the beginning of the statement, we can see Mrs Laing gives us some personal details and she says that her husband was certified as having died of

Hepatitis C-related liver disease. They appear to have been married for 52 years, around 52 years, before he died and he had worked as a linesman for Hydro Electric. Mr Laing had surgery in 1990 for bowel cancer and his surgeon was Mr Keenan, working at Forrester Hill Hospital, which I should say is also known as Aberdeen Royal Infirmary. Her husband made a good recovery and we will come on to see that he did have a blood transfusion at that time.

Mr Laing continued attending outpatients for five years after that for follow-up, having had bowel cancer. After he had really finished that period of follow-up, he was told that there was news in relation to Hepatitis C. He was told that he had contracted Hepatitis C. I may say this information about how he learned of the virus is perhaps not quite what is reflected in the records but Mrs Laing has a recollection of him being told by Mr Keenan that he had contracted Hepatitis C through the blood transfusion he had received in 1990.

He didn't say much about it. Then if we look at the next page, from that time on, he attended his GP every six months for blood tests and again he didn't really discuss that with Mrs Laing.

Mr Laing did, however, relay to his wife the

information that there wasn't a lot that could be done for the Hepatitis C. He could have treatment but his understanding was that it wouldn't make much difference and it might make him worse:

"My husband didn't discuss it any more and just got on with his life."

So someone who plainly didn't make any fuss and was very stoical about what had happened. She is not sure if he was referred to any other doctor and she says in paragraph 7, the only time that she was actually aware of the Hepatitis C issue was that when Mr Laing had a cut, he would always tell people to stay away. So he was plainly very vigilant about any risk of transmission to his family.

Then she charts a deterioration in his health from the year 2000 onwards and then particularly in 2003, over the summer, if we can go on to the next page, he really became very unwell and spent some time in Woodend Hospital. Then he went home and then went back to Aberdeen Royal Infirmary in July and then back into hospital and then at the end of August Mrs Laing was told that there was no more that could be done and in fact, although he was supposed to be going to move from the Royal Infirmary, he did die before that happened. So he died in Aberdeen Royal Infirmary on 4 September.

Mrs Laing records that her husband didn't tell anyone apart from family about the Hepatitis C and they feel that it shortened his life.

So having conducted that review of Mrs Laing's position, I would like now to lead the evidence of Dr Graeme Alexander.

THE CHAIRMAN: I take it, gentlemen, you are content with that narrative?

MR DI ROLLO: Yes, thank you.

MR SHELDON: Yes, sir.

DR GRAEME ALEXANDER (affirmed)

Questions by MS DUNLOP

MS DUNLOP: Good morning, Dr Alexander.

A. Good morning.

Q. Can I ask you, first, before we look at your report, to look at your CV, which is PEN0020704. There it is. Can you see it on the screen?

A. I see the first page.

Q. Yes. Just to perhaps highlight one or two things about your curriculum vitae. You are currently a consultant hepatologist in Addenbrookes in Cambridge. Is that correct?

A. Correct.

Q. You have occupied this position since August 2003?

A. I have been in Cambridge since 1991.

Q. Right. I'm just wondering what the reference is -- if we look to page 3. Is that just the name of the trust?
A. I changed positions in the same hospital.
Q. Right. So you were the clinical director of hepatology. What's SDU?
A. Service delivery unit.
Q. From May 1991 to July 2002 and then clinical director of gastroenterology, hepatology. This is just renaming of the departments, is it?
A. A slightly expanded role, but, yes.
Q. From July 2002 until October 2004. So where does the consultant hepatologist bit fit in?
A. All the time, alongside.
Q. So these are, as it were, more administrative roles?
A. Yes.
Q. You graduated MBChB from Bristol in 1976?
A. Yes.
Q. I see you did an MD. What was your MD on?
A. Viral hepatitis.
Q. B and C?
A. No, unfortunately C hadn't been identified then. I was too old for that.
Q. Right. And you tell us that you were, in fact -- and this is on to the fourth page, next page, please -- born in Ayr, in fact?

A. Yes.
Q. You must have left Scotland at quite a young age?
A. I had the accent beaten out of me at quite a young age.
Q. You started out as a research assistant in oceanography?
A. Yes.
Q. But you tell us that wasn't for you. You decided on medicine.
A. I didn't know what I wanted to do when I left school.
Q. Just to go through your CV, you have -- and this will be about another three pages on -- a list of peer-reviewed publications, yes, which you have organised for us on an annual basis. We can all see -- particularly those of us who have a hard copy -- that there is a very significant number of publications, listed in the hundreds, plainly almost all of them in relation to viral hepatitis. Then at the end I see a section headed "Original papers". This is the second last page. Sorry, if it is difficult to find. Yes, original papers lost their way. Are these unfinished or ones that you didn't publish or what?
A. Usually research fellows never finish the papers that they were supposed to finish.
Q. So in your day-to-day job, you are involved in caring for patients with liver disease?
A. Indeed.

Q. Teaching on liver disease?
A. Indeed.
Q. And also some administrative duties?
A. Less administration now.
Q. Thank you. In that capacity -- that is the teaching and caring rather than the administration -- have you been asked to look at the treatment of a patient called Alexander Black Laing?
A. Yes.
Q. And you have prepared a report, I think, on Mr Laing's care?
A. Yes.
Q. Is that right? Perhaps we could have your report, which is [LAI0011125]. The first page gives us just a little bit of background on your expertise. Obviously we have been discussing and could we go, please, to the second page, which gives some background on Mr Laing.

Dr Alexander, I would like to go through this with you also looking at the medical records, so that we can all see for ourselves what was happening at particular points. So I'm going to flag up particular pages of the records, which should appear on the screen in front of you.

The first subject you address is that Mr Laing developed bowel cancer and was referred to a surgeon,

Mr Keenan at Aberdeen Royal Infirmary in the middle of 1990. Perhaps we could look at [LAI0010127], please. This appears to be a discharge letter dated 20 August 1992 to Mr Laing's general practitioner. I just wanted to ask you a couple of questions about this letter.

Mr Laing has had anterior resection. Obviously that must be at the front, some tissue has been removed. Is that correct?

A. Yes.

Q. To put it in colloquial terms: and the ends joined together?

A. Yes, anatomically intact, as it were.

Q. Unfortunately, says Mr Keenan -- this is a Duke's C. Could you explain what Duke's C means?

A. Yes, this is an internationally agreed classification of the severity of a carcinoma, giving us an idea of how far the cancer has progressed at the time that the operation was performed. This tells us that the cancer has moved from outside the bowel, beyond the local territory into lymph glands some distance away, and that's the type of cancer operation that carries the worst prognosis in the longer term and the highest chance of recurrence.

Q. What would be a lesser grade? Would it be a different

letter?

A. A is the one with the best outcome long-term and B is an intermediate one.

Q. Thank you. Mr Keenan said it had also invaded one of the seven glands?

A. Yes.

Q. So in general terms with carcinoma, if it has spread into the glands, this is a worse feature?

A. There is a much higher chance that this disease would recur at a later date.

Q. Mr Keenan is saying that the glandular spread, having involved only one of the glands, that may be a slightly better prognosis.

A. Yes.

Q. Can we go to 1995, please, and go to [LAI0010105], please. This is a letter from Aberdeen and Northeast Scotland Blood Transfusion Service dated 26 April 1995. It is actually a letter from a Dr Yates, who is a consultant in that centre, to Mr Laing's general practitioner. In broad terms what seems to be happening here is that the blood transfusion service are contacting Mr Laing's GP to say that it has been discovered that the blood Mr Laing received in his cancer surgery in 1990, came from a donor who had Hepatitis C. Is that correct?

A. Almost correct. What has happened is that the blood donor has been back to give blood a second time or third time, and on the subsequent test he has been found to be Hepatitis C positive. The assumption has been made that he was positive, or she was positive at the time of the operation, of the first donation.

Q. I appreciate the point you are making is that in fact the infection which has been picked up could be of very recent standing?

A. Could be.

Q. Yes, but nonetheless recipients of the blood are being followed up and going to be offered testing?

A. Yes.

Q. And this is known as the look-back exercise?

A. Yes, I actually chair the steering group for that exercise.

Q. For how long have you been chair of the steering group?

A. Since the beginning.

Q. And that's a UK-wide steering group, is it?

A. Yes.

Q. So this procedure would be what you would expect as chair of the steering group?

A. Absolutely.

Q. What Dr Yates is saying to the general practitioner is -- if we can go down the letter a little bit:

"The patient will need to be approached with a view to counseling and testing to determine his HCV status. If you are willing to undertake this role, we will provide details of the blood samples needed and where these should be sent and offer any further support or advice. If, on the other hand, you would like us to notify and counsel the patient, we are happy to do so."

The doctor, Dr Yates, is enclosing a questionnaire for Dr Lynch to complete. Can we turn to the next page, please? There seems to be a possibility that the GP may feel that telling the patient is not advisable and that would be something that could be stated and followed up, but in this case that didn't happen?

A. Correct.

Q. Can we go to the next page, please? I should have gone backwards. It is [LAI0010103]. This is the questionnaire. If we just go down and see that some basic biographical details are enclosed, and then if we go to the next page, 104, that is what Dr Lynch is being asked to complete in relation to Mr Laing. Is that correct?

A. Yes.

Q. We can see from the middle in response to question 5:

"Do you wish to undertake the counselling yourself," the GP has said "Yes".

The next stage in this is at [LAI0010019] and this is Dr Yates writing back to Dr Lynch having received the questionnaire, saying that Dr Lynch is willing to take responsibility for the counselling and testing and some further documents are being sent for his assistance in that task:

"The nationally agreed counselling guidelines ..."

Are we to take it from what you have told us that these are the UK-wide counselling guidelines?

A. Yes.

Q. And then a form to document the outcome of the process. Can we look at [LAI0010102], please? What Dr Lynch did was to write to Mr Laing and ask him to come in. I suppose it must be difficult for GPs to strike the right note when sending a letter of this kind?

A. Yes, particularly at that time, we didn't know what the risk of transmission was.

Q. Right. So I suppose the task is to include enough to communicate the information the patient has to have, without making them, at least at this stage, unduly anxious. Is that a reasonable summary?

A. Absolutely.

Q. We can deduce from the sequence of events that Mr Laing did as he was asked and came in because if we look at [LAI0010101], the page before, the GP is writing and

saying that he has the results of the blood tests:

"Perhaps you could pop up and see me and we will discuss matters further."

So the GP is obviously feeling that this is information that has to be communicated face-to-face?

A. Correct.

Q. Then if we see the page before that, [LAI0010100], the GP is, as he has been asked to do, reporting back to Dr Yates to say that:

"Mr Laing has tested positive for HCV antibody and his Hepatitis C serum is reactive and the confirmation test is positive."

It seems to have been not quite as Mrs Laing remembered it: that he had already been discharged from Mr Keenan's clinic. He seems to have been on the verge of discharge from follow-up for his bowel cancer and then this has come along:

"I have told him that he seems to have contracted Hepatitis C from his transfusion and that it may or may not damage his liver and that he will be seeing a specialist to advise about the possibility of interferon or not. He accepts all this with equanimity."

Is that last paragraph a reasonable forward plan?

A. It is a very fair plan.

Q. Right. It appears that Mr Laing was being very philosophical about what had happened.

A. Yes.

Q. Of course, we know, because we have actually already looked at the set of guidelines that's in Mr Laing's records, that a lot of information is provided to the GP about what topics to cover in the counselling of the patient.

Can we look at [LAI0010098] and LAI0010099. 98 is difficult to read. I think because it has been quite a thin tissue, would be my suspicion, but just in broad terms, we can see that this is a request for hospital care and that the nominated clinic is the gastrointestinal clinic with Dr Sinclair as the consultant. This relates obviously to Mr Laing because his details have been filled in. If we look at the back of the form, which is 99, we find the narrative:

"Please see this 72-year old gentleman who has Hepatitis C."

And that he had got it from a blood transfusion in 1990.

Then the GP provides a little more information and says that:

"Mr Laing is in perfect health and he doesn't have any hepatomegaly."

In other words, his liver is not enlarged.

A. Can I just check the date on that one? Is it 99 or is it earlier.

THE CHAIRMAN: I think there may be confusion with the reference numbers, Ms Dunlop.

A. I think it's 1995 or 1996 from my recollection.

MS DUNLOP: Actually, it's not immediately obvious to me. I think it is the summer of 1995 but I can't immediately see the date. Yes, there we are, 12 July 1995.

So from the previous documents it looks as though Dr Lynch had seen Mr Laing, I think in June 1995 and this is a referral going, in July of 1995, to Aberdeen Royal Infirmary.

A. Yes, quite promptly.

Q. The next event in the sequence is shown on [LAI0010095] and this is a report back to the general practitioner from the gastrointestinal and liver service at Aberdeen Royal Infirmary. Mr Laing has been seen by Dr Sinclair and one of his team. Then there is a report of the plan. What is being done when the doctor says:

"We are going to be doing a PCR test to see the activity of the virus."

A. Okay. If you are infected with Hepatitis C, a small proportion of patients will clear the virus immediately and they are left with an antibody which can be detected

many years thereafter before fading. That suggest that they have cleared the virus and are no longer at risk. The majority of patients -- and it is a higher and an older age group -- remain positive for infection and you can find the virus in blood. The PCR refers to the type of test done to look for the virus genetic material in blood. It is called a polymerase chain reaction.

Q. Thank you. Dr Cox, who I think, if we go down just a tiny bit, was a senior house officer in the clinic, is saying that the problem with this patient is his previous Duke's C tumour?

A. Yes.

Q. What is the thinking here? What's the problem?

A. He has been alerted to the abnormality of liver function tests and his first assumption is that the cancer has recurred, I would guess, and he wants an urgent scan of the liver because that would pick up a secondary from the original cancer. I don't think he is requesting an urgent test from the Hepatitis C point of view. That was my inference.

Q. I take it again that that's an understandable train of thought, is it?

A. Perhaps. The liver function test wouldn't have suggested recurrent disease, it would be more consistent with Hepatitis C. But I'm not sure an SHO would be the

right person to make that decision.

Q. In any event the effect of it is possibly going to be slightly over-cautious?

A. The appropriate investigation has been done if not for the right reasons.

Q. Yes. [LAI0010092]. This is Dr Sinclair writing from the gastrointestinal clinic saying, in the text of the letter, that he can't yet see the PCR result and that the long-term outlook with Hepatitis C, in someone of this age group, is probably fairly benign:

"There will probably be a significant amount of time before he produced enough chronic liver damage to create ill-health. My guess is he will die of something other than liver disease."

That didn't turn out, in fact, to be true but was it a reasonable enough hypothesis at this point, in November 1995?

A. I think there are two issues here. First of all, I think even at that stage, recurrence of his cancer would have been more likely than not in the longer term and it is not unreasonable to say that might have carried him off. In 1995 we didn't have really good insight into the natural history of Hepatitis C and particularly in the older age group. Any evidence we had at that stage suggested that it was a ten-year lag

to 20-year lag before cirrhosis would kick in. So it is not an unreasonable assumption in the light of information in 1995. We now know that's wrong. That's not the case in 1995.

Q. Right. First of all, we are told that the consultant's view is that Mr Laing has seemed completely unfazed. But in any event, Mr Laing is not communicating that he is very anxious or concerned, one can deduce, but nonetheless Dr Sinclair says:

"We are due him a clearcut opinion as to the state of his liver and the only way to do this is with a biopsy."

A. Yes.

Q. But I think we can follow the logic that if the PCR test had been negative, it wouldn't be necessary to do a biopsy because it would mean that he had cleared the virus.

A. Again, that's what I would certainly do now or would have done for the last ten years. In 1995 we were still biopsing people, even if the PCR was negative, because we weren't confident of the reliability of the test.

Q. But as far as the possibility that there has been metastasis from the bowel cancer is concerned, there seems to have been good news on that.

A. Yes, indeed.

Q. Can we go, please, to [LAI0010089]. In fact, he has had a liver biopsy. The letter was on 17 November. He had it in January 1996. It has been an uncomplicated procedure. Can we scroll down, please? We have the liver biopsy results appended to this letter. The liver biopsy has shown chronic active hepatitis. It looks difficult to be certain, the appearances are suspicious of cirrhosis.

I think you cover in your report, Dr Alexander, that what was said in the biopsy by the laboratory, and what the physicians said about the biopsy are not quite the same.

A. Agreed.

Q. It is worth looking at this stage at the biopsy report, which is [LAI0011009]. Holding in our minds that that letter had said the appearances were consistent with cirrhosis. Can you just talk us through this then, please?

A. Yes, I assume the court is familiar with the liver biopsy. It is a piece of tissue obtained by sticking a needle into the liver. When you get a good piece of tissue -- it is about 1 to 2 centimetres long and about the thickness of a Bic biro, the inside of the biro that contains the ink -- that would be a really good sample. So samples fragments of tissue of 0.2 and 0.3 centimetre

are very, very small, and thin strands of tissue -- I think it says elsewhere in the report that thin strands of 0.9 centimetres and 0.5 centimetres are not a good sample of liver tissue. The possibility here is that, because the liver was scarred -- this is hypothesis -- that the scar tissue gets left behind and the softer tissue come out with the needle, and that's what's sent to the pathology department.

So when you see a fragmented biopsy you know immediately that you can't rely on the findings absolutely and that you may be underestimating the amount of scarring. And the histologist who has looked at this has that in mind, I'm quite certain, when he is making his comments. He also comments that there is distortion, in the second paragraph down, the third line from the bottom:

" ... distortion of the vascular relationships with mild thickening of the liver plates."

They are features that you see in cirrhosis and you don't usually see short of cirrhosis. So although he has got very little tissue, he is suspicious that this is cirrhosis without the full picture being available to him. He is also commenting, in the last paragraph, about chronic active hepatitis, which means the degree of inflammation, which again would be more marked in

someone who had cirrhosis than someone who didn't.

I think what has happened is that at a later date, the pathologists and clinicians have sat down together and talked it through and come to a different conclusion.

Q. In that discussion, the conclusion they have come to is that things are slightly less bad. Is that correct?

A. Yes.

Q. But your own view is that the impression you would get from that report was probably accurate?

A. But I have always worked on the assumption that you take the worst possible news when making clinical decisions rather than the best possible news, and if the pathologist is suspicious you have got cirrhosis, that's a reasonable thing to follow, but people work in different ways.

Q. Yes. Can we go back to the sequence of events and look at [LAI0010088]? Is this where the process of perhaps slightly understating the biopsy is beginning?

A. Yes, I think so.

Q. So where the third sentence says:

"His biopsy shows chronic active hepatitis with mild fibrosis."

You are saying that you would have thought it probably was cirrhosis?

A. It probably did show mild fibrosis because most of the

fibrosis was left behind. But this is guesswork. My instincts and the pathologist's report suggest to me that he probably had cirrhosis in 1996.

Q. The second paragraph covers the topic of treatment, and Dr Sinclair, the gastroenterologist, has been involved in the discussions but, says the writer of this letter, Dr Bhutta:

"In view of his age and having no symptoms with only mildly abnormal liver function, we are not keen to start him on interferon. We will discuss his biopsy at the pathology conference."

Then there is going to be further monitoring. We will probably come back to this, I think, Dr Alexander, but you have no quarrel with what is said here about the possibility of interferon treatment, do you?

A. I think it was a difficult decision to make and I think it was a decision that had to be and has to be made in conjunction with the patient.

Q. Yes. Can we look then at [LAI0010083]? We can see that that discussion has taken place. Dr Sinclair says:

"I discussed the options with him regarding this and if anything, he preferred to take his chances and not have any interferon at all. I think this is a very reasonable suggestion and I have discharged him."

Would that have been what you would have done, you

would have sat down with Mr Laing and had a discussion about interferon?

A. Yes, and the biopsy and the future.

Q. It is accurate to state, as at September 1996, is it, that there is a relative lack of success of interferon?

A. I think it is more than that. I mean, our own data over a ten year period showed a success rate of less than 9 per cent across the board, and when we reviewed it in about 2001, 2000, people over 60 didn't respond at all. It is pretty foul to take as well. So I think you have got to balance up: he had little to gain and a lot to lose by being treated.

Q. Thank you. If we look at [LAI0010087], so two pages further on, Dr Lynch, the general practitioner, is continuing to discharge his responsibilities in that he is going on keep an eye on Mr Laing's liver function tests and it looks as though the plan is to check them about every six months. So the patient is being asked to come in at the end of the year and there is going to be some more testing done. Is that reasonable?

A. Yes, I think some of us do it differently. Because I have a big research interest, we follow up all our patients forever and that's an expensive way of doing things. Often the GP is the best placed person to look after someone, particularly for someone in their 70s who

might not find travelling to hospital easy.

Q. I wanted also to look at [LAI0010067]. Look at this. The date isn't immediately leaping out at me. The important thing about this for our purposes is to note that this is a request for an outpatient appointment at a dental clinic and the reason is given in the letter. The reason is that Mr Laing needs some dental work but his own dentist has declined him treatment because he is Hepatitis C-positive. That happens, does it, Dr Alexander?

A. All too often, unfortunately.

Q. Could you give us a little more explanation of what happens when people are turned down by their own dentists?

A. They are usually advised to find an alternative dentist and we are fortunate -- I think most teaching hospitals are fortunate -- in having a dental practice on site and they take on the care of our patients with Hepatitis B and C that dentists won't see.

Q. So there are some dentists who simply won't treat a patient who is Hepatitis C positive?

A. Yes.

Q. And is that because they are concerned about infection transmission?

A. I assume so. I don't know the answer to that. There is

an anxiety among some dentists that they might be dealing with people with liver disease, who have got low platelet counts and a high prothrombin time, two things that happen with liver disease that predispose you to bleeding, but as there is no information about clotting in the letter, I can't assume the dentist has made that decision based on concerns about bleeding.

Q. I see in fact I have noted that this letter is from September 2000. That must be on there somewhere but I am afraid I can't at the moment immediately see it.

A. He is 76 in the referral letter.

Q. I see, yes, but I think there must be something in the letter. It is sometimes not very easy to see when you are looking at it on the screen. But, yes, 76.

Yes, there we are, found it. It is at the very bottom, 4 September 2000.

Now, back to other aspects of Mr Laing's health. If we look at [LAI0010057], we can see that this is December 2001 and there seems to have been a question of gallstones. So this is him back having had obstructive jaundice, which at this point seems to be more likely due to gallstone disease than to his hepatitis. Is that right?

A. That's what the letter says. It is not, I think, what was happening.

Q. Well, can we look at the second page of the letter?
A. The blood tests are not consistent with that diagnosis, nor was the ultrasound.
Q. You think that this was the hepatitis, rather than gallstones?
A. I think it is a manifestation of liver failure, an early manifestation of liver failure due to his Hepatitis C, yes.
Q. I suppose in fact there is some commonsense support for this, in that no gallstones were noted in the gall bladder?
A. They can be missed. Ten per cent of gallstones are missed in this context but there was nothing to suggest that was the likely cause.
Q. Now, [LAI0010052] takes us on to June 2002, and we can see that Mr Laing has been referred to a hepatitis clinic and seen by a specialist nurse and a Dr Fraser. So it looks as though, as well as the gastroenterology service, there is are a specialist hepatitis clinic. Do you know Dr Fraser?
A. I do.
Q. And the clinic is running with at least one specialist nurse as well and he is having a number of different problems. Do you think those problems are related to the hepatitis?

A. He has got a past history of duodenal ulceration, so it might be a mixed pattern, but I think many of the symptoms would be readily attributable to evolving liver disease.

Q. But one of the things that we should note from this letter is that he still apparently does not wish to be treated for the Hepatitis C.

A. Yes, that's a consistent pattern.

Q. Then, that being the middle of 2002, can we look at [LAI0010038], please? We can see this is another referral letter, this time to Woolmanhill hospital, and can we just scroll through this, please?

LAI0010039. We can see from this, firstly, that Mr Laing is suffering from gynaecomastia, thought to be due to his cirrhosis. In fact all three of the gentlemen whose records we have looked at this week, who have all had Hepatitis C, have all had gynaecomastia. Is that something that one finds in patients who have Hepatitis C.

A. It is a feature of advanced liver disease rather than Hepatitis C per se.

Q. Can you explain the mechanism, please?

A. Yes, there are changes in the balance of hormones in your circulation, and men and women both have androgens and oestrogens, the male and female hormones

respectively, but the way they function is dependent on how much of the hormone is free to act. So if it is bound to something, it can't act but if it becomes free it can.

In advanced liver disease you have more oestrogen free, whether you are a man or a woman, so you start to develop more female characteristics: You lose some body hair, you become sexually less potent and you develop breast enlargement, which can be noticeable.

Q. Is it perhaps slightly offbeam to think it was due to the psoriasis?

A. It is not psoriasis, it is a misspelling. It is a common misspelling in medical records of cirrhosis.

Q. I see.

A. I suspect.

Q. Thank you. The penny has just dropped. I was very puzzled when I saw that.

Thought to be due to cirrhosis.

A. Yes.

Q. It's quite a difference.

A. Oh, yes. It is a common mistake.

Q. And then, in relation to other features, the general practitioner is reporting that he has had the loss of appetite, weight loss, nausea and vomiting, been seen at Dr Fraser's clinic and then and he has continued to have

nausea and vomiting and a bit of swelling and abdominal distention. He has also developed some tremor. It does actually look from the medical records, Dr Alexander, as though this may have been Parkinson's?

A. Impossible for me to comment on that but I would guess, based on the other symptoms that he has got, that we are looking at advanced liver failure, with hepatic encephalopathy which characteristically comes with unsteadiness of gait and a tremor.

Q. Is that known as "liver flap"?

A. Yes, but without examining him, I can't be certain. But I would be pretty confident that's the likely cause, not a superimposed illness.

Q. We can see that he has a tremor in both hands and it increases on intentional movement.

A. Yes.

Q. Can we just look at the final page, please? We can see from that he is really not taking very much alcohol either.

Now, the next document I would like you to look at is [LAI0011020]. We can see there has been a CT scan of the liver in July 2003. Perhaps you could just highlight for us the significant findings from the scan.

A. Okay. The liver is small. What happens with most liver disorders is that initially the liver becomes enlarged

and then, as the process evolves over years or even decades, the liver shrinks down and then becomes too small to sustain life.

The liver is described as "irregular", which means that the surface of the liver has a scalloped contour, which would be consistent with cirrhosis.

"No focal lesion" means they are looking for liver cancer and can't find it.

It is surprising the spleen is not enlarged. It often is in advanced liver disease. Then also he has got moderate ascites. This is a collection of fluid in the abdomen, which is suggestive of liver failure and from a clinical point of view tells me that life expectancy is less than two years, and on this occasion he has got gallstones, which were missed previously on the ultrasound. So these really tell me he has got advanced liver disease.

Q. And indeed if we look next at [LAI0010031], we can see that the picture from the end of July, when that scan was done, was one of a steady deterioration.

A. Yes.

Q. I have asked someone else, Dr Alexander, about decompensated, and we have been told that it means that a condition which has been under control is no longer under control. I don't know if you would agree with

that.

A. It's a fair description.

Q. Right. Of course, it wasn't really under any form of active control?

A. No. It really means the presence or absence of the complications of liver disease that carry morbidity and mortality, which include bleeding, which he had had, ascites, which he has now got, and confusion, which he has now got.

Q. Right. What is pedal oedema? Is that swollen feet?

A. Feet, yes, a feature of liver disease.

Q. What's the mechanism whereby patients such as Mr Laing become encephalopathic?

A. A million-dollar question.

Q. All right.

A. We know that blood ordinarily is processed from the gut through the liver and the liver does something to the blood that takes something out of the blood so that when the blood is delivered back to your heart and brain, it is good for you. In liver disease the blood doesn't go through the liver, it goes round the liver, because the liver is scarred and presents an obstruction to flow. So something in gut gets into the blood, which gets into your brain or whatever, by not going through the liver in liver disease, which causes confusion.

Q. Is this controversial?
A. No, it is just not understood very well. We know some of the compounds, for example, ammonia, but we don't know quite what to target.
Q. Ammonia is neurotoxic, as I understand?
A. Yes, it is one of the compounds that we can find in association with encephalopathy, probably not the only cause.
Q. Then we can see that the medical staff have realised that Mr Laing is not well enough to go home and they were thinking that he might go to another facility but there wasn't time for that and he began to fade, and if we look down on the letter, we can see someone has written on that he died on 4 September.
A. Yes.
Q. So he was in hospital for a little over a month in his final illness.
A. Yes.
Q. Then can we look at [LAI0011068], please. We looked at several death certificates this week, Dr Alexander. This one only has one thing shown as the cause of death: Hepatitis C-related liver disease. That is accurate, is it?
A. Yes, insofar as it goes. I think liver failure, secondary to Hepatitis C and cirrhosis, would have been

how it should be filled out. It is as accurate as it needs to be in terms of communicating the cause of death.

Q. So you would have included perhaps a bit more explanation of the sequence of events?

A. Yes.

Q. But as a summary of what the cause is, this is fine?

A. It is clear, yes.

Q. That was the pathology report we looked at. The biopsy report; we have already looked at that. I wanted to go back to your report, please, having just had a bit of a look at some of the landmarks along the way. Can we go to page 2 of [LAI0011125]. A paragraph that begins:

"I could find ..."

As I think we saw at Dr Sinclair's clinic, there seem to have been discussions of the possibility of treatment, and at least once also at Dr Fraser's clinic, and that the patient was not keen and you have already given us your views about what the prospects for treatment would have been. Then you have covered the possible gallstone incident in December 2001. If we go to LAI0011127, you have dealt with Mr Laing's final illness in 2003.

I think we perhaps understand the terminology there now from the other people whose case notes we have

looked at, but ascites is this collection of fluid and peripheral oedema, swelling in his feet mainly, jaundice, which is the sort of yellow colouring which is to do with bilirubin. Is that right?

A. Indeed.

Q. What is it actually? What's the mechanism that gives you jaundice?

A. Again, not very clear but essentially bilirubin is being pumped back into the circulation rather than being cleared by the liver. It is a sign that the liver is failing and injured and it is a natural response of the liver to injury.

Q. Is it cachexia?

A. Wasting. In advanced liver disease, the body starts to use your own fat and your own muscle as a source of energy, rather than food. So you lose muscle bulk and you lose all your fat and look very thin, it is a feature of late, late disease.

Q. Portal hypertensive gastropathy?

A. Yes, your blood, as I alluded to earlier, normally travels from your gut into a very soft liver. It is a low pressure system. If your liver becomes distorted and scarred, it is hard for the blood to get from the gut into the liver. It starts to go backwards rather than forwards and finds other routes. So the stomach,

which is downstream of the pressure effect, becomes very distended, thickened with blood, which can bleed quite readily; high pressure in the gut makes it bleed.

Q. We note too that he had oesophageal varices. We have been thinking of those as internal varicose veins. Is that reasonable for lay people?

A. Exactly. And these are the veins that are distended by the high pressure in the system because of the scarring and distortion in the liver. It is like standing on a hose downstream of the high pressure.

Q. Thank you. You go on to say that there is very little that's contentious, chart the surgery in 1990 and the look-back and the testing and the ascertainment that Mr Laing had developed Hepatitis C, and then seven years later he died. You say in the following paragraph that the short interval -- just six years between acquisition of the virus and documentation of the cirrhosis and then the seven years, 1996 to 2003, that followed his death:

"Are consistent with what we now know about the natural history."

I understand that in younger people these periods can be considerably longer.

A. Many young people don't get cirrhosis at all, if they are young at the time of infection, the time of exposure. In fact, the majority do not.

Q. What about the period from the development of cirrhosis to end stage liver disease?
A. In younger patients that would be of the order of ten years or more. The older you are, the shorter that period. So both the period between evolution to cirrhosis and then the evolution from cirrhosis to death are shorter in people who are older when they are first exposed to Hepatitis C.
Q. You comment that the first large publications drawing attention to the importance of age were published around 1997. I take it this is publications in which a large number of people had been studied?
A. Yes, enough to make you understand the natural history of Hepatitis C in older patients was not as we had first thought.
Q. What did you first think? Is that the comment that it was expected to be relatively benign?
A. I think most of our experience was based on what was called non-A non-B hepatitis, which is transfusion-related liver disease, prior to the introduction of Hepatitis C testing. In those circumstances the majority of people died of diseases related to the reason they had a transfusion, not to the hepatitis that arose as a result. So we had an artificially skewed view of what Hepatitis C -- then

called non-A non-B hepatitis -- did to patients, and it wasn't until the introduction of testing for Hepatitis C in 1991 that we realised there were a lot of people out there that had much, much different disease to that which had been described previously, and the penny dropped about five or six years later.

Q. Just to digress slightly into a general point and I don't think it does any harm to emphasise this, it isn't the case, is it, that there was an identified virus that was called non-A non-B hepatitis and it just changed its name to Hepatitis C?

A. No, no.

Q. They were different types of diagnosis, is that correct?

A. Non-A non-B hepatitis was simply abnormal liver tests that arose after a transfusion, of which there are numerous reasons.

Q. So for doctors and scientists, it was question of trying to find what was causing non-A non-B hepatitis?

A. Yes. The clinical context, there was not much you could do; and the science context, people would take blood from those patients and try to infect, for example, a chimpanzee, and show that that blood was infectious to a chimpanzee. But the number of experiments being done was small and the number of patients exposed was high. So the clinical scenario and the scientific work were

quite separate really.

Q. And we are going to try and come back to this in much more detail later in the Inquiry, but at the end of the 1980s, 1988/89, the Chiron Corporation were successful in finding the Hepatitis C virus. In other words, they found another virus causing non-A non-B hepatitis?

A. Yes.

Q. It is not terribly well put. If I could change that. They found another virus causing hepatitis and that was the virus that was the culprit --

A. Yes, it was the main cause of infectious transmitted hepatitis with transfusion.

Q. Thank you. The conclusion of that paragraph that we were just looking at about the short interval, is that the information that was provided to Mr Laing at the time of his biopsy was probably best known practice, and do you remain of that view?

A. I do.

Q. We see in the next paragraph you mention the 9 per cent figure that you told us about earlier. Really, I suppose a very disappointing success rate for treatment with interferon at that time?

A. Yes, and for treatment that's very unpleasant to take. So it is a miserable year on treatment. To take a year out of someone's life when they are 72 is something you

would have to take very seriously for such a low likelihood of success.

Q. You comment that you think the biopsy was underreported?

A. Yes.

Q. Does that really mean that you think the lab report on the biopsy --

A. I have to emphasise I haven't seen this, and I don't think it has been reviewed by a pathologist outside Aberdeen. But I think the biopsy's features, as reported by the pathologist, reflect cirrhosis, and with hindsight, that's clearly what he did have at that stage because that's how the disease evolved thereafter.

Q. Yes, I just wanted to clarify that perhaps, just so that we understand where the underreporting crept in. Really, it was in the way that the report was interpreted subsequently by the clinicians?

A. My guess was that there was what is called a clinico-pathological conference, which is usually attended by the clinicians involved and the pathologists. There might be one or two or maybe up to a dozen people in the room, and a discussion would have been had which was along the lines of: this is guess work; he is very well, he doesn't have any signs of liver disease, there is nothing to suggest cirrhosis clinically; at which point there is a compromise that he

doesn't have cirrhosis. All teams do that. It is good practice.

Q. It is very important, though to, ask, Dr Alexander whether you think, even if that was a slight underestimate, that made any difference?

A. I think there was a slight underestimate. I think the pathologist's report is quite clear that there were features of cirrhosis, but it would have made no difference at all to his clinical management. If I had seen him in 1996, I would have slanted my discussion with him towards not treating him. And if I saw him now, with better drugs available, I wouldn't treat him now, because treatment would give him a very low prospect of success, even with current therapies.

Q. And indeed, you say exactly that on the last page of your report.

A. It is good to be consistent.

Q. You say:

"If he had presented now with pegylated interferon and ribavirin available, the chances are he would not respond to treatment, and if I was asked now to consider treatment, I would very likely not offer him treatment because of his age and cirrhosis and the low probability of a response."

A. Yes.

Q. The only other thing to take from what you say here, Dr Alexander, is your comment about the outcome from the Duke's C carcinoma.
A. Yes. It is not my territory but 13 years after a Duke's C is an impressive survival, but again you might want to go back and look at the original histology and confirm that that was correct, but it is a good outcome and the surgeon did well.
Q. I think finally, Dr Alexander, I should ask you to have a look at a letter that we have, sent to the central legal office by Dr Sinclair. It is [PEN0100174]. Just a one-page letter from Dr Sinclair. We will see he is now at Albyn Hospital in Aberdeen, and much as you had guessed, the biopsy was reviewed at the clinical-pathology conference, pathological conference:

"The severity of the changes were thought on consensus to be rather less than initially reported."

We have covered that. Then Dr Sinclair charts further attendances by Mr Laing at the clinic. Discussion of treatment. There is a final paragraph -- I don't know, you have maybe not seen this letter before. I suspect you haven't seen it, Dr Alexander, have you?
A. I saw it last night.
Q. Oh, you saw it last night?

A. Yes. I think the letter is a very fair review of what has happened and I think if it had been me in his position, I would not have treated the patient.

Q. Yes. The final paragraph, or at least the paragraph that begins:

"It is possible ..."

A. Yes.

Q. Dr Sinclair is really getting into something that really was never going to be possible.

A. You can't have hindsight at the time, useful though it would be.

Q. He couldn't have been aware of data because the data weren't available.

A. Yes.

Q. And he couldn't have offered combination therapy because it wasn't on offer.

A. I think the care Mr Laing was offered was exemplary actually.

Q. Thank you very much, Dr Alexander.

THE CHAIRMAN: Dr Alexander, can you help me a little bit with the relationship between age and the time lapse between infection and cirrhosis?

Is there a shape to the curve we have been working in?

A. We have been working in the lab on the effect of aging

and outcome, and what we have been doing is measuring your biological age. Within your DNA you have a mechanism that prevents your DNA being damaged, and you have on the end of your DNA pieces of DNA which look a bit like a shoelace with a piece of plastic on the end. So your shoelaces have a piece of plastic on the end to stop them fraying, and the DNA in your body has a piece of plastic on the end [sic] to stop the DNA from fraying. Because if you damage your DNA, you get cancer. As you and I, unfortunately, get older, our telomeres get shorter and we then start to get cancers, cardiovascular disease and strokes, the disease of aging.

We now know that in Hepatitis C positive patients, your telomeres shorten and you become unable to mount an immune response to the virus when you hit a certain age. The boys in my lab find it very amusing when the age for treatment cut-off was 58, which was the age I was when we did the work. So your immune system stops working when you get to around 60, and if you do not have an immune system, you can't cope with the virus. So the virus takes a stronger grip.

THE CHAIRMAN: So 60 is, in some way, a step change because by that stage your biological time clock has run a significant part of its course?

A. Yes, we weren't designed to live until 60.

THE CHAIRMAN: I sometimes wonder why the Cabinet Secretary was right to take me, over 70, and absorb several years of my life in this.

A. I couldn't possibly comment.

THE CHAIRMAN: Mr Di Rollo, there is quite a lot of complexity there; there is nothing you wish to follow up?

MR DI ROLLO: No, thank you.

THE CHAIRMAN: Mr Anderson?

MR ANDERSON: I don't know if we need the microphone, it is a very short matter.

We looked at this letter of 1995, part of the look-back process. It may be common knowledge but can you help us with when the look-back process started?

A. It started being considered virtually the minute that the Hepatitis C testing showed that some donors were positive. You may or may not be aware that the majority of blood donors who are Hepatitis C positive, in the past, have dabbled with drugs. One assumes that when you ask blood donors to come forward, they are asked about drug use at that stage. They are supposed to not come forward if they are going to give blood. What has happened is, for example, you might have a blood transfusion service turn up at a supermarket or

a workplace where people can't not go forward and give blood because there is pressure on them and they would have to declare their reasons for not giving blood.

So these people get into the system and continue to give blood. So we actually were surprised in 1991/1992 how many blood donors were turning up positive. We hadn't anticipated as many people would acquire Hepatitis C from transfusion as eventually were found to be positive because the majority of patients don't get ill with Hepatitis C.

So from about 1992/1993 onwards there was a group working -- and I was part of that group -- to see how we would manage it to ensure there was a national standard, and we wanted to, from the scientific point of view, find out as well what happened to these patients. So it took between 1993 and 1995 to get the process off the ground nationally but we did start looking in 1993.

MR ANDERSON: The letter we saw was dated 1995. Those sorts of letters that were being sent out, would they be sent out in 1995?

A. Yes.

Q. Was that the same in Scotland and England and Wales?

A. It was a national programme. So when a good donor came back to the service to donate blood a second time and was then found to be Hepatitis C positive, that alerted

us to the fact that he or she had given blood before, and each of the persons who had received blood previously would then be screened or offered screening.

You will imagine that not everyone comes back and gives blood a second time, so not all the people who have Hepatitis C have been identified even now. We are still seeing the odd person coming to clinic now. And not all the people who received blood from those donors have been able to be tracked because they have moved. So there are still people here and in England who have got Hepatitis C from a transfusion that we don't know about.

MR ANDERSON: I'm obliged to you, thank you very much, sir.

THE CHAIRMAN: Mr Sheldon?

MR SHELDON: Not for me.

MS DUNLOP: I just want to not let Dr Alexander go without clarifying something that I couldn't quite hear. Is that all right?

It was just to go back to the shoelaces, Dr Alexander, if we could.

A. Sorry.

Q. I'm looking at the transcript. There was a piece of plastic on the end of the shoelace which is there to stop it being damaged?

A. Frayed.

Q. Frayed. What's that called?
A. I don't know.
Q. You used a word which I couldn't hear?
PROFESSOR JAMES: It's a telomere.
A. No, the telomere is the piece of DNA but the piece of plastic on the end of the shoelace also has a name. The DNA is the genetic material; the telomere is the bit on the end of your DNA which is equivalent to the piece of plastic on the end of your shoelaces.
MS DUNLOP: Could you spell that for us, please?
A. T-E-L-O-M-E-R-E.
THE CHAIRMAN: I suppose all we have to think of as former Boy Scouts and Boys Brigade boys is the need to take a bit of nylon rope and seal the ends so that it doesn't unravel.
MS DUNLOP: You can do it with Sellotape as well.
THE CHAIRMAN: Sellotape wouldn't give the permanence needed in someone of my age.
MS DUNLOP: So that's the protective bit at the end of the DNA. I think that was the bit I was puzzled about.
Thank you very much.
THE CHAIRMAN: Professor James, I think you are trying to console me that some people still have significant telomere when they are 75.
A. I think he is trying to console himself that he has a

very long one.

THE CHAIRMAN: Dr Alexander, thank you very much, you have been very helpful.

MS DUNLOP: I think it is time for a break.

THE CHAIRMAN: I think so.

(10.53 am)

(Short break)

(11.40 am)

MS DUNLOP: Sir, I should apologise for the time taken at the break. I was having some extra coaching from Dr Dow.

THE CHAIRMAN: I'm sure it will save us time now.

MS DUNLOP: That's my hope.

Right, can we have Dr Dow now, please.

DR BRIAN DOW (sworn)

Questions by MS DUNLOP

MS DUNLOP: Good morning Dr Dow.

A. Good morning.

Q. We are going do ask you some questions obviously but first of all I would like to have your CV on the screen. It is PEN0130421.

Dr Dow, you work for the Scottish National Blood Transfusion Service. What's your actual job title?

A. I have retired. I was head of the

Scottish National Blood Transfusion Service microbiology reference unit. I do work obviously as a contractor to SNBTS, Penrose team.

Q. Where is the microbiology reference unit?

A. Initially it was in Ruchill Hospital in Glasgow and then Law Hospital at BTS West. It is now currently within Gartnavel BTS West.

Q. Is that within the West of Scotland specialist virology centre?

A. That was the regional virus lab away back in the 1990s, when it was actually formed, the microbiology reference unit. It moved out of the virus lab in 1998 to Law Hospital, when they moved to Gartnavel.

Q. Thank you. Can we look at page 2, please. We see that you are originally from Perth?

A. Yes.

Q. It looks as though you started out going to be a vet?

A. I was.

Q. But you changed your mind.

A. I changed my mind and they changed my mind.

Q. Right. You went into bacteriology, and that's, what, a subspecialisation, or a majoring in virology and medical microbiology. Is that right?

A. Yes.

Q. And then you worked in the department of infectious

diseases at Glasgow University doing a PhD on non-A non-B hepatitis in the West of Scotland?

A. I did that as part of my work with the Blood Transfusion Service. As you see below, I have worked for the Blood Transfusion Service since 1974. So it was a part-time PhD.

Q. So even though it was part-time, you managed to do it in five or six years?

A. Well, that is about the time you have to take it when you do it part-time. It is quite slow.

Q. I was meaning it really seems quite quick. Some people take ten years or more?

A. Full-time PhDs are usually in three years.

Q. Then we have a list of your publications. And finally your supplemental list. What's different about those on the supplemental list?

A. There is not quite so good journals, as such. Some of them are actually letters. The Lancet publications tend to go in there as well because they are just letters to the editor.

Q. I see. You have a list of committees as well. Keep going through, we can just see. Yes, committees, quite a lot there. Some Scottish, some UK like NIBSC. That would be a UK one, is it?

A. Well, it is an international one.

Q. And obviously WHO too. That's an international one?
A. Yes.
Q. Then your memberships of your professional bodies. Even something called the Scottish Viral Hepatitis Group?
A. I think that's nearly defunct now.
Q. Was it multidisciplinary?
A. It was, yes.
Q. And what was that, just a sort of --
A. It was --
Q. -- information and knowledge sharing?
A. In the early days of Hepatitis C, in the early 1990s, a group of individuals came together, people from Health Protection Scotland, what was then SCIEH.
Q. What was SCIEH?
A. The Scottish Centre for Infection and Environmental Health. And gastroenterologists, the likes of Henry Watson attended, Peter Brunt from Aberdeen, David Goldberg from CDS, SCIEH as such, and others.
Q. Then you had some teaching appointments as well.
A. Yes.
Q. Good, thank you. You have provided some information in relation to a Mr Alexander Laing. Is that correct?
A. Correct, yes.
Q. Just to recap. We know that Mr Laing was contacted in connection with the Hepatitis C look-back exercise

because it was identified that he had received blood from someone who was found to be Hepatitis C positive?

A. Yes. That's correct.

Q. We also know that it turned out that Mr Laing had acquired Hepatitis C from the blood transfusion that he had had with blood from that donor.

A. Yes.

Q. Mr Laing received his blood transfusion in August 1990 and that was a time when donated blood was not being screened for Hepatitis C in the United Kingdom. Is that correct?

A. That was correct, yes.

Q. Right. So the question arises whether, if screening had been in place, the donor's Hepatitis C could have been picked up and by that means Mr Laing's infection prevented. Do you understand that?

A. Yes, I understand that, yes.

Q. We need to have your documentation in front of us. It is [PEN0010016]. You give us some narrative. You were discussing Mr Laing's case within the SNBTS Inquiry team and you raised a query about the particular genotype of Mr Laing's Hepatitis C. Is that right?

A. That's correct, because obviously we knew that the genotype was quite important in relation to the generation of test.

Q. Yes. You couldn't find what his genotype had been from his own records but you did get that information by researching the donor's genotype. Is that right?
A. That's correct, yes.
Q. And the donor's genotype is genotype 3?
A. Yes.
Q. Dr Dow, this material is challenging for those of us who are not qualified in the way that you are qualified and what we are going to try and do is give ourselves enough of an understanding to follow the story insofar as it relates to Mr Laing, but not so much information that we all get lost. Do you understand that?
A. I hope I can help, yes.
Q. So what we are going to do is, I'm going to ask you some questions and they are going to be leading questions. If I'm understanding what you are telling us, then I hope that my understanding will be shown to be correct and that you will be able just to assent to what I'm going to suggest. I should say, obviously, you and I have met before, not just today but on another occasion, so I have had the advantage of some coaching on this.
A. Yes.
Q. If we could start by saying that all organisms are made of cells. Is that correct?

A. That's correct.
Q. Right. Inside a cell will be the genes for an organism?
A. That's right.
Q. All the genes together form the genome of that organism?
A. That's correct, yes.
Q. You could also, therefore, describe the genome as the genetic complement for that organism?
A. You can.
Q. Although, I think your preference would be to call it the genetic code?
A. Correct, yes.
Q. But it is the totality of the genes for that organism.
A. Okay.
Q. A virus is an organism. So a virus has a genome?
A. Correct.
Q. That genome determines, for the organism, what it is and what it does.
A. Yes.
Q. The mechanism by which it does what it does is through the manufacture of proteins, and RNA is involved in that, but I don't really want to get into what RNA is. It is a messenger. Is that fair?
A. That's fair, yes.
Q. Right. Tell me if you feel uneasy with anything.
Insofar as what the organism is and what it does are

concerned for a virus, what it does is to make people ill?

A. Usually.

Q. Well, certainly in the case of hepatitis.

A. Hm-mm.

Q. Enter antibodies. An antibody is a protein. Is that correct?

A. Correct.

Q. It is something produced by the human body to neutralise part of the virus.

A. Yes.

Q. Correct?

A. Correct.

Q. That antibody will be a necessary but probably not sufficient part of a successful immune response.

A. That's true, yes.

Q. Right. If I have been infected with a particular virus, my body needs to make enough of the right kind of antibody, which are needed to defeat or neutralise the virus, if I'm going to defeat the virus, if I'm going to clear the virus.

A. Usually that's the case but there is also -- T cells are involved as well.

Q. That's why I said it is a necessary but not sufficient part.

A. Correct, yes.
Q. We have mentioned genotypes. Different genotypes of a virus are slightly different genetically but not different enough to be a different virus. Is that fair?
A. That's pretty fair, yes. It is like looking at people in general. We have Asians, we have Africans, black, and we have Caucasians, who are white. The same with the Hepatitis C virus; there are different genotypes.
Q. We are all people.
A. Yes.
Q. Right. We have mentioned genotype 3. A person who has successfully thrown off -- fought, cleared -- genotype 3 Hepatitis C has been able to manufacture enough of the right kind of antibodies, those proteins, to neutralise Hepatitis C virus genotype 3. Is that right?
A. Yes, it happens very rarely, though, that the virus has actually cleared completely.
Q. Right. When we talk about antibody testing -- I'm saying "we" although obviously it is not something I would ever be able to do -- we are looking for an antibody as a clue that the virus has been here?
A. Correct, yes.
Q. Is that right? The problem, as I understand it, with the first generation antibody tests was that they were much better at recognising antibodies to genotype 1 than

they were at recognising antibodies to genotype 3?
A. Yes, that's very true.
Q. Right. Equipped with that kind of Ladybird guide, can we look at what you say?
THE CHAIRMAN: Is there perhaps a need for the ladies and gentlemen who have never heard a tutorial from Dr Dow to try to highlight one or two of the principal elements in it, Ms Dunlop.
MS DUNLOP: That's what I was going to do.
THE CHAIRMAN: I think it is the problem that giving a lot of information as quickly as that, some of it may get lost, and I was just wondering if Dr Dow can bring out the essence of this. I think that we would get the message that viruses sometimes cause illness, that the immune response to viruses is generally to try to develop antibodies, if that happens, that sometimes the antibodies are effective in clearing the virus, but with particular viruses the prospects of that are very remote.
A. Correct, yes.
THE CHAIRMAN: And that applies in particular to Hepatitis C.
A. And in particular to Hepatitis C, yes.
THE CHAIRMAN: However, even within that generality, there are some types of antibody or some types of genomic

sequence in the virus that make them more difficult to deal with than others.

A. It is a very hard thing, all this, to actually try and explain to people who don't know anything about it.

THE CHAIRMAN: You are now finding that it is difficult to explain it to me.

A. I did actually produce six slides, the colour slides that are in front of some people, and that actually gave a potted version of what this is all about.

THE CHAIRMAN: I have got them, and we may get to it, but at the moment we are trying to get the overhead picture.

Essentially, what is it, when we come to genotype 3, that causes the problem here? Can you put that in a nutshell?

A. The genotype 3 was not detected by first generation tests. That's what we realised. Very few people who were infected with genotype 3 were actually detected by the first generation tests and this is because the first generation tests were directed against the NS4 region of the virus. It is a non-structural region of the virus. It was only against this particular area, and for some reason or other, the virus itself -- the different genotypes don't actually see different areas. So the components used for first generation tests could only detect genotype 1 and didn't really detect many

genotype 2s or 3s very well at all. It was mainly by cross-reaction that they were detected. That's why it was important to actually identify the genotype of the donor involved with patient Laing.

THE CHAIRMAN: I don't suppose it would have been known very early on, when you were testing, that there were genotypes that were escaping the net.

A. No, we didn't know at all, although I did do a report on the first generation tests, which in our hands was a lot poorer than what the Americans were claiming in their investigations of post-transfusion hepatitis. We didn't know what was happening but we certainly couldn't get the same percentage of individuals that we could identify related to post-transfusion hepatitis.

THE CHAIRMAN: Has that got to do with different incidence of genotypes in different places?

A. That's correct, yes, and that's why this genotype is quite important here.

THE CHAIRMAN: Ladies and gentlemen, there is no way that I'm going to make the whole thing clear to you; I'm going to have to study it later. But perhaps by osmosis we will develop an understanding as we go on.

MS DUNLOP: Yes. Dr Dow, can we go back to what you have produced for us and look at that? I'm looking at the third paragraph. We see that your research was able to

identify the donor, who has a particular reference number, and that's a person whose virus type had been genotyped as genotype 3, with strong four-positive antibodies to a particular region of the virus.

If we try to translate that into perhaps lay terms, the measurement for 4 plus is a reflection -- you say "strong" antibodies. It doesn't mean that they are particularly muscly antibodies, it just means there are a lot of them.

A. A high concentration, yes.

Q. Right. So this particular individual had a high concentration of particular proteins because we established earlier that an antibody is a protein?

A. Yes.

Q. And those particular proteins were being involved in the fight against the virus?

A. Yes.

Q. That was their job?

A. Yes.

Q. Right. But those particular antibodies were not so successfully picked up by the first generation test?

A. They weren't picked up at all by the first generation tests because the first generation test didn't have any C22 or C33 components within them. They were based solely on 5-1-1 and C100, which are NS4 components.

Q. But in our lay terms the first generation test wasn't able to recognise those particular antibodies?
A. They wouldn't see it at all because they weren't there.
Q. Right. And the chairman has alluded to different distribution of genotypes. I'm not necessarily going to go through your slides in consecutive order but it is interesting to look at the individual slides. We don't have these in court book, sir, partly because of difficulties of reproduction. It was felt that actually hard copies were better in this instance.

Now, Dr Dow, just a moment ago you talked about initial research, and this is in the early 1990s, is it, in which you were involved?
A. I'd been working at non-A non-B hepatitis before that, in the 1980s.
Q. Indeed, but the assembling of information about Hepatitis C has been a step by step process, has it?
A. Yes.
Q. And at the beginning, almost by definition, people didn't know that there were different genotypes?
A. Correct, yes.
Q. Right. I don't want to -- I shouldn't really digress at all but what's the current state of play? How many genotypes have been found?
A. Well, some people would say there is a lot more but we

would still say there are only six.
Q. Right. Just to boggle our minds ever so slightly more, those six, some of them are subdivided?
A. Quite a few of them are subdivided, like 1A, B, C, 3A, B, C, D, and others. So there are subdivisions but the subdivisions are not so widely divergent as the main genotypes.
Q. That makes sense. That's like the British person with red hair and the British person with black hair, to take your "we are all people" analogy a bit further?
A. That's right, yes.
Q. You said that earlier in the story of testing poorer results were being obtained in the United Kingdom than were apparently being obtained in the United States and his Lordship suggested to you that that was something to do with the distribution of the different genotypes?
A. It was, yes.
Q. So, for example -- and this is perhaps in retrospect -- knowing now that the first test is particularly good at recognising genotype 1 --
A. Yes.
Q. -- the first test is going to produce very good results in a country where there are a lot of genotypes 1s?
A. That's correct. North America was in that situation.
Q. Right. For Scotland -- now, I think you do have your

percentage -- we have got a wee map of Scotland actually.

A. Overall Scotland, 50 per cent were genotype 1, 10 per cent were genotype 2 and 40 per cent were genotype 3.

Q. Right, thank you, that was what I was looking for and couldn't immediately see, but within Scotland even we see that the picture varies, and that's page number 6.

A. Yes, within that we have got -- bottom left is Northern Ireland. We also did the confirmations for them. The histogram above that is for Glasgow and above that was Inverness. On the right-hand side is the east coast: Aberdeen, Dundee and Edinburgh areas.

Q. It is interesting in the context of the enquiry we are making today to notice that for Aberdeen the representation of genotype 3 is quite low.

A. Quite low, yes. It is the exception that proves the rule.

Q. Yes.

A. These were just what we have done from the initial 100 or so donors we had, these histograms, and it still panned out that way. Even now the levels are still roughly the same as what I have just stated.

Q. Yes. And you did some research on -- you tell us yourself. If we look at page 3, there are some nice

coloured pie charts.

A. Yes, the pie chart relates to us trying to retest the first 100 or so Hep C positives we found amongst our donors by first generation tests. We subdivided them according to genotypes 1, 2 and 3, obviously, and you can see from the pie chart that 90 per cent of the genotype 1s were detectable by the first generation test, (inaudible) first generation test, and only 70 per cent of genotype 2 and almost two thirds of genotype 3 were not detected by first generation tests.

Q. So if we look at the blue, basically, 90 per cent type 1s were found by the first generation test, 30 per cent type 2s were found and 32.5 per cent type 3s were found?

A. Correct, yes.

Q. So if you were either type 2 or type 3, the odds were that your hepatitis wasn't going to be found --

A. Correct, yes.

Q. -- by the first generation test.

A. And that was the case with the donor involved with patient Laing.

Q. Yes, because in relation to that individual, the quality of the information is actually even better, so we should go back to that.

As part of your research project, you say this:

"Furthermore -- " if everybody can see that, slightly more than half way through the biggest paragraph:

"Furthermore, on 12 March 1992 as part of a small research project we tested T2103, along with 49 other HCV-positive donation samples, and found this sample to be negative with the first generation test."

So the actual donor who gave the blood in 1990 that was transfused to Mr Laing, you tested in 1992 using the first generation test?

A. Correct.

Q. The purpose of that was to see what would have happened if first generation testing had been in use in Aberdeen in the summer of 1990, and the answer was that this individual's virus would not have been picked up.

A. Yes, the donation at that time, had it been screened by the lab, the first generation tests would have been completely negative. We would have banked the blood and used it, and that's exactly what happened. We didn't have a test at the time. But had we had the test, it would have been negative anyway.

Q. Perhaps we could look at slide 2. As I understand it, what is shown here is the result of testing ten different people with the second generation test. Is that right? Samples from ten different individuals?

A. Yes, it is the confirmatory test that we used to actually confirm samples that were reactive in the ELISA test for Hepatitis C.

Q. Right. Really, the point of this slide, I suppose, is firstly to illustrate how it works.

A. Yes, and the donor involved in patient Laing would have given a practically identical pattern as number 7.

Q. Right.

A. Which shows that there is no reaction against 5-1-1 or C100, which are first generation components.

Q. Okay. So if we take an individual sample -- take patient 6, for example.

A. Yes, that looks like a genotype 1.

Q. Right, okay. What is being shown by this strip with the bars on it?

A. These are antibodies against different areas of the Hepatitis C genome.

Q. So for patient 6, his sample, when tested, the test is picking up these different kinds of antibodies, so antibodies to different parts of the virus?

A. Correct.

Q. Is that right?

A. Yes.

Q. And actually there are four of them. It is picking up all four and you are saying that on the basis of that,

you can say that that's probably a genotype 1?
A. Correct, yes.
Q. But for patient 7 only two kinds of antibodies are showing up, C33 and C22, because that's what's well represented. There is a high concentration of those antibodies in this patient but it is not picking up the antibodies to 5-1-1 or C100 and you are saying that that very strongly suggests that that is a genotype 3 person?
A. It would likely be, or a genotype 2.
Q. Yes, and because with the first generation tests you didn't have anything below the third row -- in other words, if this had been the first generation test, you didn't have --
A. We didn't have C33 or C22 components.
Q. So if this had been the first generation test, the bottom of the picture would have been a line underneath C100?
A. That's right.
Q. Right. And so for this person, patient 7, that area of the strip would have been blank.
A. Completely negative, yes.
Q. Yes. You felt you wanted to do some more research, Dr Dow, on these donors, I gather, and you looked at what is termed "surrogate testing" as well?
A. Yes.

Q. Or you looked at the constituent parts of surrogate testing. By surrogate testing, do we mean looking for markers that might indicate the presence of a virus?
A. In a way that's the case, yes.
Q. If you would rather put it in other words, please do?
A. Really we are looking at tests which aren't directly related to Hepatitis C itself. We are looking at other assays that may give us an indication that it may well have been infected with Hepatitis C, but really it wasn't conclusive. One of these was ALT, the other was anti-core for Hepatitis B. Obviously, the anti-core test is an antibody against Hepatitis B; it is nothing to do with Hepatitis C at all.
Q. The thinking behind this is perhaps not so difficult. It is just that observation has shown that in patients who have Hepatitis C there is a high correlation with raised levels of ALT, which we know is a liver enzyme.
A. That's right, yes.
Q. And there is also a reasonable correlation between having Hepatitis C and also having this Hepatitis B core antigen?
A. Quite a lot of our drug abusers on the West of Scotland had evidence of both Hepatitis B and Hepatitis C, and obviously a lot of our Hep C-positive donors actually admitted to having been intravenous drug users a long

time in the past.

Q. So you are looking for other things that are often found in people who have Hepatitis C.

A. Right, yes.

Q. And when, with this collection of donors, you looked at raised ALT, you found that ALT, the raised ALT measurement, would have picked up a certain proportion of these donors?

A. That's correct, yes.

Q. And I think you say in your paper what the proportion would have been. I have to find that. Do you remember offhand?

A. It varies according to genotype.

Q. Right. Overall?

A. Overall, I would have to look at my -- I think it was about 60 per cent at one point, we thought.

Q. If we look at the foot of page 9 of the article -- I should have said that you published -- this is [PEN0010018] -- you and others published an article on all of this research on the donors, which should come up on the screen.

If we look at the third page into the article, please, and if we can go to the bottom of the page, please, we see in the second last line of the right-hand column that a total of 27 of the 90 donations you were

able to test for ALT had normal ALT values?

A. It is about 30 per cent, yes.

Q. Yes. And were also anti-HBc-negative. Is that right? Now, I think for this particular donor you weren't actually able to do the ALT comparison.

A. That's right. We tried to find out if it was included within the 90 and it wasn't.

Q. Yes. So we don't actually know what would have happened if some sort of surrogate screening, involving looking for raised ALT, had been employed in the summer of 1990.

A. We don't know.

Q. We don't know because you didn't do that measurement for that donor?

A. Correct.

Q. So all we really have to go on is the overall statistics?

A. Yes.

Q. And we can see that more than half of the 90 donations would have been picked up as having abnormally raised levels of ALT?

A. That's true, yes.

Q. In fact, immediately above the passage dealing with the 27, we should look at what was said about the breakdown of the different genotypes, and you found that for genotype 3 ALT levels were significantly higher than

genotypes 1 and 2. Is that correct?

A. That's correct, yes.

Q. And you say that also in your rubric. You say:

"The distributions of alanine amino transferase levels ..."

That's ALT.

A. Correct, yes.

Q. "... were significantly different in those infected with type 3."

So, looking at that overall picture, it does look as though, if ALT screening had been in place, there is quite a likelihood that this donor would have been picked up.

A. You can only surmise that.

Q. Yes. But I think the same was not true for the anti-HBc?

A. The anti-core was negative.

Q. You were able to measure that with this individual?

A. We had the specimen so we were able to do that. ALT has to be done at the time the specimen is collected usually because the ALT will drop off, so it has to be done fairly fresh.

Q. Yes, and that takes us into another area, which is that with this piece of research you were measuring the ALT, or if you had had this donor and were able to measure

his or her ALT, there would have been quite a significant time interval; you would have been doing it at least two years after.

A. Yes, it wouldn't have been valid.

Q. What about that principle in relation to the actual antibody test? Could somebody test differently two years apart?

A. No. If somebody is PCR-positive, the anti-body will be continually being stimulated because the virus in the blood will be stimulating the T-cells to continue producing antibody. So the antibody won't go off. If the PCR became negative, the antibody will wane over several decades.

Q. I think we did have some discussion of this before today and you said that, in relation to this particular donor, the result with the first generation test was a long way short of what would have been the significant levels. So even a sort of fluctuation that one might get from day to day would be unlikely because this result was a long way below?

A. Yes, the level was well away from the actual cut-off point that we may require to make something reactive.

Q. Yes. It is quite interesting, in connection with the whole idea of the ALT testing, to look at slide 5 -- picture 5?

A. That's taken from the same paper, obviously.
Q. Yes.
A. It is within the paper.
Q. And this is really a way of showing in a graph what might happen if one used ALT testing, at least on this collection of people.
A. Correct, yes.
Q. Right.
A. And also healthy donors because it is within that.
Q. Okay. Each dot that we can see on this graph is a person. Is that right?
A. Yes.
Q. Or perhaps, to a scientist, each dot is a sample?
A. Correct.
Q. Right. And the row along the top are normal healthy donors?
A. Correct, that were negative for Hepatitis C.
Q. I should say -- and we have had some mention of this before -- there are two kinds of tests. There is a screening test, which picks up people who are likely to have active virus, and then there is the PCR test, which definitely picks up active virus.
A. The PCR test will actually show that people have viremia.
Q. So row 1 are normal healthy donors, screen-negative

donors. Row 2 are people who screen positive?

A. They are confirmed antibody Hep C positive, not just screened.

Q. Yes, but on PCR testing they are negative?

A. Correct, PCR-negative.

Q. And rows 3, 4 and 5 are people who both screen and PCR test positive?

A. Correct, according to a genotype.

Q. So they are people who have Hepatitis C, and you have got their genotype: 3, 2 and 1?

A. Yes.

Q. So you say in your narrative that HCV antibody positive/PCR negative individuals -- and that's line 2, row 2 -- are very similar to normal screen negative/HCV negative donors?

A. Yes.

Q. So are you really saying that the distribution of the dots as compared between line 1 and line 2 is quite similar?

A. Very similar.

Q. Yes. And then, when we look at lines 3, 4 and 5, this vertical line here is the upper limit of normal?

A. Yes, it is.

Q. So all the donors to the right of this line would be rejected?

A. Correct, yes.
Q. And to the left of the line would be accepted?
A. Yes.
Q. Right.
A. You can see that 3 per cent of our normal healthy donors would be rejected as well.
Q. But we can also see that a certain number of people who do actually have the virus are on the left of the line.
A. Correct.
Q. So it is quite a useful visual representation of how well or otherwise ALT testing would work as a surrogate marker.
A. That's true, yes.
Q. Right. We have already really mentioned this but your research was written up and published as a paper, which is the article we looked at in a journal called "Transfusion" in 1993.
A. That's true, yes.
Q. I think you actually published one or two other papers or letters in relation to this, did you?
A. Yes, there was a publication in the Lancet before that, describing the RIBA patterns, which were slide 2. Obviously we realised there were different patterns there and that's what led to genotype 3 being discovered by SNBTS and it has been patented by BTS.

Q. So genotype 3 has been patented?
A. Correct. Yeah. I don't think we have made much money out of it, though. We tried to do the same as what Chiron did, they have patented the Hepatitis C virus and perhaps all the litigation should be with them.
Q. I think perhaps those of us who were taught about patenting inventions might struggle with the idea of patenting a virus, or a genotype of a virus, but that's a discussion for another day -- or perhaps not.

Just to go back to your paper, [PEN0010016], you say in terms what we were talking about a moment ago, and this is:

"Furthermore ..."

You say in terms what you said in evidence, that looking for the Hepatitis B core antigen didn't work with this particular individual as a marker?

A. No -- yes, I think you said "Hepatitis C core".
Q. No, I said Hepatitis B. I did mean to say B.
A. Sorry.
Q. Looking for anti-HB core, this particular individual was negative on that test, and then you say, unfortunately ALT had not been performed.
A. Correct, yes.
Q. If we turn over to 17, your conclusion is that:

"First generation testing of this donor in July 1990

would have resulted in a negative result and the donation would still have been cleared for use. Had surrogate anti-HBc testing been performed, it would also have resulted in a negative result."

Then for C, because you don't have the actual result for this donor, you just say:

"If first generation tests had been in use in July 1990, 61 per cent of donations found reactive with second generation testing would have been detected."

A. That's overall.

Q. That's overall. But that's really the best we have in relation to this particular donor.

A. Yes.

Q. Can I just ask you, Dr Dow, about this donor, just a couple of questions. I know that the Blood Transfusion Service, for absolutely understandable reasons, is very careful about the confidentiality of information relating to its donors, but when this donor was identified, was there any sort of information obtained which would help to explain how this donor might themselves have got Hepatitis C?

A. Each Hepatitis C positive donor was obviously asked to come back for counselling by our donor consultants and I tried to actually create a database of all the Hep C positive donors, the risk factors, that they may have

had to explain how they had been infected with Hepatitis C, and this particular donor actually admitted to having had a transfusion at some point in the past, either the 60s or 70s.

Q. So to a degree, it is speculation but one might speculate that that was the way that the donor --

A. We could speculate that but there could be other reasons as well. Certainly that's a possibility. Obviously we recorded that as the risk factor for this particular donor.

Q. Finally, can we just look at [PEN0110003]. That's really a question on this point. It doesn't mention the fact about having had a blood transfusion previously.

A. No, I think we were asked about higher risk donors, and really, as far as transfusion goes, we have only recently barred donors who have had transfusions in the past, and that was roughly about 2002 I think this happened and it was in relation to variant CJD exposure.

Q. But what might you have considered or what were considered to be high risk groups in 1990?

A. Would be intravenous drug use; a man who had had sex with another man would be a high risk group.

Q. And you were able to say that in relation to this person, this person did not fall into one of those groups?

A. He didn't fall into any of these groups. We questioned this at the session and also at counselling as well. So he had been answering negative to these questions on two occasions.

Q. Well, I'm being told that the evidence about the graph wasn't very clear. So I think perhaps we should have another go at the graph.

A. Is this number 5?

Q. Yes, slide 5, please.

A. Can I walk through it, no?

Q. Perhaps I can tiptoe, can I?

A. Okay, then.

Q. Right. Along the bottom, the horizontal axis of the graph, is measurements of ALT, so how much ALT there was in each individual sample, how much of that liver enzyme there was. Is that right?

A. Correct, yes.

Q. A vertical line has been drawn about a third of the way along the graph to show the level of that liver enzyme beyond which measurements would have been regarded as abnormal?

A. Yes, anything to the right of that would be classified as abnormal, but to actually classify somebody as having hepatitis would be three or four times the level of that upper limit of normal.

Q. So this is quite a cautious setting of normal --
A. Yes.
Q. -- to try and pick up as many positive donors as possible? Right.
What have been plotted on to this graph are a large number of dots, with every dot being a sample from an individual?
A. Correct, yes.
Q. So for every one individual, what their measurement of that liver enzyme was has been plotted on this graph?
A. Yes.
Q. Right. And they have been plotted according to five different categories of people?
A. Correct.
Q. The first category is people who, on a screening test, tested positive for Hepatitis C?
A. No, tested negative.
Q. Sorry, tested negative for Hepatitis C. So they are, as you put it, I think, "normal, healthy donors"?
A. Correct.
Q. So that's the people at the top, the first row, and to the left of their dots we see HCV?
A. Yes.
Q. The second row are people who didn't pass the screening test --

A. The second row are actually people who are confirmed Hep C positive and have been counselled.
Q. I haven't finished. They are people who didn't pass the screening test but when the further test, the PCR test was used, it passed that.
A. No -- well, they didn't have virus circulating in their blood.
Q. Right. So they are a different group of people. They have not passed the screening test?
A. They are still confirmed Hep C positive, as far as antibody tests go, right. So they have been infected with Hepatitis C. It is just that there is no virus in their blood.
Q. So they are likely to be people who have had the virus and got over it?
A. Hopefully.
Q. That takes us back to the discussion at the beginning about how antibodies work and so on.
A. Correct.
Q. So they don't have virus circulating but rows 3, 4 and 5 are people who fail the screening test and are also found, on the test for circulating virus, to have circulating virus?
A. Correct.
Q. And they have been split into different groups according

to the genotype of their virus.

A. That's right.

Q. So we have genotype 3, 2 and 1?

A. Yes.

Q. And looking at the graph, we can see where all those individuals end up on the graph. As you would expect, a very large number of the normal healthy individuals have normal levels of ALT.

A. Correct.

Q. And they are all the people whose dots are here on the top left-hand corner of the graph.

A. That's right.

Q. Then the next group of people, the people who were failed on the screening test, if you like, but didn't have circulating virus, that's their dots here and most of them -- in fact, is it all but one of them? -- are also in the normal section of the graph.

A. That's true, yes.

Q. As far as their ALT measurement is concerned.

Then for genotype 3, the people who actually had active Hepatitis C infection and who were genotype 3, most of them -- and that's all the dots to the right of the line on the type 3 row -- had abnormally high levels of ALT?

A. They were above the upper limit of normal, yes.

Q. Because they are to the right of the line. For type 2 it looks much closer to 50/50.
A. Yes.
Q. Some of them had normal levels of ALT but some of them had abnormal levels, higher levels of ALT. Then, in relation to type 1, what's the split? Maybe about two fifths, three fifths. So two fifths of them had normal levels of this liver enzyme and maybe about three fifths of them had abnormally raised levels.
A. Yes.
Q. So it actually looks that for type 3 the ALT test, surrogate test, is reasonably effective at picking up the people who have got type 3?
A. Yes, it is partly related to the previous figure as well, which we haven't actually gone into, but that shows the genotypes according to age of the donor.
Q. You had better tell us about that, that's slide 4?
A. Within that slide, the very top component is those people who are antibody positive but are PCR negative; in other words, they have been infected with Hepatitis C but have no circulating virus, and we can see that there there is nobody under the age of 25.
Q. Yes.
A. Which is quite important. Whereas in the genotypes below that, we see that genotypes 1 and 2 have

individuals of roughly all different ages. Genotype 2 tend to be slightly older but genotype 1 probably represent the Scottish donor population, the way it was stratified at that particular time but genotype 3, we don't have any donors over the age of 40. That relates to, obviously, genotype 3 has been recently introduced into Scotland as opposed to genotypes 1 and 2, which have been around for a lot longer.

Q. That's presumably, at least in part to do with demographics and sociology.

A. Yes.

Q. And population movement.

A. Population movement, yes.

Q. People settling here from other countries and bringing their viruses with them.

A. And there is people who have been elsewhere in the Second World War and could have been returned with the virus and spread it as well. Who knows? But it has been roughly since the Second World War that genotype 3 has come in.

The PCR negative ones, these people who are PCR negative are a bit older. So they have had the infection and could well have spontaneously got rid of the virus. They are still antibody positive.

Q. Thank you very much, Dr Dow?

A. Okay, thank you.
THE CHAIRMAN: Dr Dow, I'm still struggling with some of the absolute basics. An ELISA test is applied to a sample of serum -- or what?
A. Yes, we test serum.
THE CHAIRMAN: What is the ELISA test? Is it a physical thing?
A. ELISA stands for enzyme-linked immunoabsorbent assay.
THE CHAIRMAN: Yes, but is it a physical thing, like a liquid or a --
A. We are looking at a reaction of an enzyme to detect antibody that has been bound onto a solid phase, and that enzyme will, on the addition of substrate, you will see a change of colour.
THE CHAIRMAN: So it is something that you add? That's all I'm trying to get so far. It is not an electrical process, it is a thing?
A. It is a thing.
THE CHAIRMAN: And the ELISA test is developed by a manufacturer.
A. Correct, commercial manufacturers have been involved with the Hepatitis C screening.
THE CHAIRMAN: And you have mentioned "components".
A. Correct, yes.
THE CHAIRMAN: So is the ELISA test material developed by

chemists who put together components in order to cover a range of possibilities?

A. That's what happened with Hepatitis C. The first generation test was only based on these two components: 5-1-1 and C100 from the NS4 area of the Hepatitis C virus, and Chiron obviously owned all this.

THE CHAIRMAN: And this was developed in America?

A. Correct, yes.

THE CHAIRMAN: And America had a high prevalence of a particular genotype.

A. Yes.

THE CHAIRMAN: So by chance, possibly, one had an ELISA developed that fitted the local circumstances rather well.

A. Correct, yes.

THE CHAIRMAN: And what happened later was that additional components were introduced that enabled the raising of antibodies across a broader spectrum.

A. Not exactly raising the antibodies, but they detected --

THE CHAIRMAN: Detected them across a broader spectrum.

A. Yes.

THE CHAIRMAN: So is the difference between the first generation and the second generation that there simply wasn't the appropriate component in the test to be able to identify the antibodies relating to what was critical

locally here?

A. It wasn't as effective as what it was in obviously North America. North America made great claims about how it solved all these non-A non-B, post-transfusion hepatitis cases. We didn't see that here in the proportion that was found in North America.

THE CHAIRMAN: I think I understand that ALT is an alternative and how it fits in, but it is a physical process one has in mind or a chemical process one has in mind, in which it depends on what you put in, what you are likely to find in the way of the ELISA test.

A. The ELISA test, obviously the antibody will bind on to whatever you put on the solid phase. So if the solid phase has the right component there, you will detect all the different antibodies.

THE CHAIRMAN: Perhaps we don't have to bother too much about binding-on and so on. The process brings up a result that demonstrates the presence of the antibodies.

A. That's right.

THE CHAIRMAN: Thank you.

PROFESSOR JAMES: Lord Penrose, could I ask one thing?

My name is Professor James, I'm the medical adviser to the Inquiry. Would it be right in saying that in the very late 1980s up to 1991, the discovery of the

Hepatitis C virus, it was really unknown whether non-A non-B hepatitis, post-transfusion, was due to one virus or maybe two or three different viruses and there was quite some controversy about this?

A. There was a lot of controversy over this, yes.

PROFESSOR JAMES: And actually what happened was that, because the initial tests in the States led to claims that, "We have found the virus".

A. Yes.

PROFESSOR JAMES: Whereas in the UK, for a while longer, it was thought that there were still maybe two or three different viruses because, in the UK, "we" could only find that this test accounted for 40 per cent -- or whatever it was -- of the cases?

A. Correct, yes.

PROFESSOR JAMES: In the event actually, there was virtually one virus but it was just a virus that had different types.

A. Different genotypes, but we know that there are individuals who have been infected by more than one --

PROFESSOR JAMES: Yes, more than one genotype, certainly, but the fact of the matter was that in the end it turned out that HCV really covered the bill for 90 plus per cent of post-transfusion hepatitis.

A. Correct, yes.

PROFESSOR JAMES: And the debates which occupied a great deal of time and thought and so on, about "Well, there must be other viruses that we haven't found yet" turned out subsequently to be almost a product of this difficulty over the genotypes.

A. A bit of that, yes. I mean, there are other viruses that can cause hepatitis and can be transfusion transmitted.

PROFESSOR JAMES: Thank you very much.

THE CHAIRMAN: Mr Di Rollo, is there anything you wish to ask.

MR DI ROLLO: No thank you.

THE CHAIRMAN: Mr Anderson?

MR ANDERSON: No, thank you, sir.

THE CHAIRMAN: Dr Dow, thank you very much. I'm sure we could do with your enlightenment at some later stage.

Ms Dunlop?

MS DUNLOP: There are no further witnesses. I should, though, draw your attention to one further document, which is [PEN0010027]. Just to draw your attention to it at the moment, I don't want to say anything particularly about it save to explain that it did seem to the Inquiry team that there was a sort of natural comparison to be made between Mrs O'Hara and Mr Laing.

We know that both seemed to have acquired

Hepatitis C through blood transfusion but that only Mr Laing was picked up through the look-back process. That meant for Mr Laing that he received a certain amount of information and counselling, and we looked yesterday at the guidelines which are in Mr Laing's records. Mrs O'Hara because she was never identified formally by a look back route, didn't receive the same level of information and counselling at all.

So to take the comparison a little bit further, there has been prepared this document which is an attempt actually to tabulate the differences between the two individuals in the sense of what information they received and what counselling they were given and indeed what follow-up was arranged for them. If we can perhaps just look through the pages in sequence, not really to go through it in any detail but just to show how it has been done.

I just would say that this was done in an attempt to produce something which might be useful to you, sir, when you were looking at what seems to be a natural comparison to be made between those two individuals because they are both very similar in terms of the time when they were recognised as having Hepatitis C.

THE CHAIRMAN: I get the impression that we have seen quite a lot of these documents in the course of going through

the history. Are they all documents that have been referred to already?

MS DUNLOP: Yes, I hope so. I mean, that can be checked, sir, we can cross-check that.

There is a further complication which I think is just inherent in the nature of this week's exercise, which is a that a lot of documents feature more than once in an individual's medical records. There may be a copy letter from the hospital, which is in the hospital records, and then the same letter is in the GP records.

There is, as you know, sir, a process the Inquiry has tried to follow of having what's called a "reference copy" for every single document with the rest being termed the "replicas", but I don't think we have actually really done that with the individual patient's medical records. So the caveat is that some of the references may be to the same document but a different version of it. But we can go back and try to standardise the references so that there is a linking possible between this table and the transcript.

THE CHAIRMAN: I'm not sure how far that level of detail will be necessary. The important thing is to be able to compare the content of the communication at various stages, and if that can be done without a great deal of

1 additional purely pedestrian work of comparison, it
2 might let you concentrate on what matters. But the more
3 comprehensive the material is the better for the record.
4 MS DUNLOP: It probably is the case that knowing the person
5 who prepared this, that this is entirely comprehensive
6 and has looked at all the letters in which an individual
7 patient's hepatitis is mentioned. We haven't looked in
8 our evidence at every single letter, but I have tried to
9 look at ones that appear to have something significant
10 about them.
11 THE CHAIRMAN: Gentlemen, are you content with this table as
12 it stands or does it require to be looked at in detail
13 by you?
14 MR DI ROLLO: I'm content with it as it stands.
15 MR ANDERSON: I also.
16 THE CHAIRMAN: And Mr Sheldon?
17 MR SHELDON: I am too.
18 THE CHAIRMAN: Thank you very much. Where are we going now?
19 Immediately I can guess, but that's not what I had in
20 mind.
21 MS DUNLOP: There are no further witnesses arranged for this
22 week.
23 We have scheduled for Tuesday what we have called
24 a "review" of the four individuals' circumstances. The
25 purpose of that is not in the sense of formal

submissions but really to try to get an idea of where we think we are with what has emerged from the evidence in relation to each person, and particularly whether there are what we have been calling "systemic issues"; in other words, have the witnesses this week revealed problems which one might call "general problems" or issues which extended beyond the circumstances of that individual and affected other people, insofar as Hepatitis C is concerned?

So, for example, the very point we have just been discussing, that there wasn't surrogate testing in 1990 in Scotland; in other words, people weren't measuring the ALT levels for blood donors to see if all of those who had ALT above a certain level should be rejected. That plainly didn't just affect Mr Laing, it affected a number of other people too and one might call that, therefore, a systemic issue. Should there have been surrogate testing in the form of measurement of ALT levels of blood donors by 1990? That really was the thinking behind Tuesday; that we would try to agree actually what those systemic issues are.

THE CHAIRMAN: So far as one can, at this stage.

MS DUNLOP: So far as one can.

THE CHAIRMAN: I imagine that factors will develop and emerge in the course of this Inquiry that might need

a revision of that. ALT is possibly quite an easy one since it has already emerged.

MS DUNLOP: I just mean systemic issues arising from the circumstances of these four individuals, because we won't be revisiting their circumstances. After that we are going to look at statistics because the whole of the exercise on which the Inquiry is engaged is better conducted against a background of having an idea of the size of the problem, and that is true both for HIV and for Hepatitis C.

THE CHAIRMAN: I would welcome that because I think that the efforts to pin that down at the preliminary report stage can't be said to have been overwhelmingly successful and it is important to try to get a measure of the problem.

MS DUNLOP: Perhaps to sign a note of warning that it isn't a straightforward task but effort --

THE CHAIRMAN: If it had been, I think we might have done a better job of it first time round.

MS DUNLOP: More efforts have been made.

We are then going to look at steps that were taken in Scotland -- or perhaps not taken -- to try to address the problem of viral infection at the first stages of blood donation. In other words, steps that were taken to try to stop people who might have particular infections from donating blood in the first place.

THE CHAIRMAN: Other than biochemical?
MS DUNLOP: Yes, almost social factors. We have grouped those exercises into two groups, firstly in relation to HIV/AIDS and secondly in relation to Hepatitis C, although there is a bit of overlap between the two. So we would hope to deal with most of those within the next three weeks and we will be having some witnesses on what we call topics B1 and C1; B1 being -- I don't really want to use the word "rejection" but it will do for the moment -- rejection of donors.
THE CHAIRMAN: I think we will see the expression "deferral".
MS DUNLOP: "deferral" is a better word, I'm obliged.

Deferral of donors on the basis of considerations related to HIV, and deferral of donors on the basis of considerations related to Hepatitis C as topic C1.

So that is our plan for the remaining part of block 1.

THE CHAIRMAN: I look forward to completing the work.

Very well, ladies and gentlemen, Tuesday morning.

(12.53 pm)

(The Inquiry adjourned until 9.30 am on Tuesday, 15 March 2011)

I N D E X