EDITED NOTES OF INTERVIEW WITH PROFESSOR JOHN D CASH, MEDICAL & SCIENTIFIC DIRECTOR OF SCOTTISH BLOOD TRANSFUSION SERVICE, EDINBURGH - 30 MAY 1990

Q. Professor Cash, please state your qualifications and professional appointments.

A. My University degrees are: MBCHB, PhD, In addition I am a Fellow of the Royal College of Pathologists and a Fellow of the Royal College of Physicians of Edinburgh. My present position is National Medical and Scientific Director of the Scottish National Blood Transfusion Service (SNBTS).

Q. When were you appointed to that position?

A. Around january 1990, but I was appointed National Medical Director of the SNBTS in October 1979.

Q. Where were you before 1979?

A. I was Director of the Regional Transfusion Centre in Edinburgh.

Q. Which appointment you took up when?

A. 1974

Q. Your primary professional interest has been what?

A. Internal medicine, blood transfusion with particular interest in products relating to bleeding disorders

Q. Who was your immediate predecessor as Medical Director before you took up your post in 1979?

A. A gentleman by the name of Major General Jeffrey.

Q. Is he alive?

A. No

Q. On 15 September 1976, you published an article in the British Medical Journal under your name and that of Mary Spensley. Can I summarize that article insofar as it is relevant to this litigation and ask, first of all, who wrote the published summary?

A. I did.

Q. In that article, you drew attention to the respective benefits and disadvantages attaching to the three then methods of treating haemophilia which were - first, fresh frozen plasma, second, cryo and thirs, AHF. Is it accurate to use AHF as another term for what I call Factor VIII concentrate?

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A. Yes

Q. The thrust of your paper was that, for patients and physicians, AHF, whether prepared nationally or by commercial companies, had significant advantages over cryo: the advantages being, it could be kept stable at ordinary fridge temperature, it was readily soluble, more concentrated than cryo and could be given in measured doses and therefore ideal for home treatment. Cryo was less stable, had variable yields, and was much less conveninet to administer in the home environment.

So those were the advantages of AHF and disadvantages of cryo?

A. Cryoprecipitate was very unpopular with some patients: for some of the reasons you have given but also the higher incidence of allergic reactions when compared to AHF.

Q. Conversely, looking at the plus side of cryo, the article brings out that the yield could, in certain circumstances be up to 60% compared with perhaps no more than 30% in respect of AHF and even less in certain countries and certain methods of manufacture. Cryo had other advantages. Cryo was quick in that you could turn it round within 24 hours as compared with perhaps up to 12 weeks for AHF. What is it down to now for AHF?

A. Cryo is slower nowadays because of virology testing. AHF remains the same. The intrinsic delay with AHF has some advantage in the context of safety.

Q. Insofar as there was an argument to be made for cryo in 1976, it was essentially a logistic argument and a financial argument - is that a fair summary?

A. Yes, but one of the main burdens of the paper was to suggest that we should not abandon cryoprecipitate until we were certain we have enough plasma to withstand the anticipated drop in yield for what clearly is a better product. If we moved in an unplanned way from cryo to AHF, it might mean we would have to buy factor VIII from commercial companies.

Q. And that was the worry?

A. Yes

Q. Was the worry directed at economics or safety or a combination of both?

A. For us, safety was paramount: we wished to minimise exposure of patients to commercial concentrates.

Q. Does the article bring that out?

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A. Probably not as clearly as it could, although I should say we were writing against the background of the WHO recommendations of 1975. This is a very important document which I suggest you read. The WHO declared that is was concerned about these safety matters and it published recommendations that each country should be self sufficient and should use unpaid voluntary blood donors for their plasma products. The article to which you refer picks up from that point and attempts to address some of the consequences of these WHO recommendations in the context of factor VIII concentrate.

Q. What was the reaction from within the profession to that article?

A. I cannot honestly say. As far as I am aware - virually zero, at least outside the Scottish Health Service.

Q. A voice in the wilderness?

A. Perhaps, but at that time there wasn't a satisfactory forum in which a corporate reaction could be generated.

Q. At the time you wrote the article was Scotland self sufficient in AHF.

A. No. One of the reasons I wrote the article was to galvanize my colleagues in Scotland to take advantage of the major investment the Scottish Office had made in building a new Fractionation Centre which was opend in 1975. It was built on the basis that "we are going to go for self-sufficiency". The published paper was, in fact, part of an invited lecture I had delivered to an international meeting in Helsinki some months before. So, in a sense, at a local level, the BMJ article was a clarion call - let's go.

Q. If we look at the chronology, the new Fractionation Centre opened in 1975?

A. It was finally commissioned in 1975.

Q. The funding would have come from the Scottish Office and not from the Department of Health?.

A. Yes

Q. If that Fractionation Centre was opened in 1975, when was it conceived?

A. I believe it was conceived and planning commenced in 1968/69.

Q. So Scotland had accepted the concept of self sufficiency many years earlier?

A. Yes, I conclude that it had. However, I should point out that I was not a Director at that time, and thus was not party to

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/to these discussions and certainly cannot take any credit. Moreover, it was never, as far as I can remember, expressed in those terms. It was always assumed in Scotland, ever since I joined the service in 1962/3, that our job was to provide all blood and blood products required for Scotland. The concept of self sufficiency more clearly emerged in 1975, against the background of the WHO report. My (personal) interpretation of self sufficiency from the WHO recommendations was that we must develop a programme which led us to advise the commercial providers of plasma products that they were no longer required. Such sentiments, of course, had political connotations and, in those days, one sensed we didn't have overt Scottish Office support for the concept of "Commercial companies go home" but we did sense strong Scottish Office support for the idea that we should get going and make as much as the Scottish Health Service patients needed.

Q. It would take some time for the Fractionation Centre to get into full production. By what date was the Fractionation Centre able to meet all of Scotland's demands for self sufficiency?

A. Some time in 1983/84. It wasn't the Fractionation Centre that was rate limiting. It was the availability of plasma. In fact, we didn't have any firm policy decisions in Scotland until we had completed a major planning review, in 1979, from which emerged our incremental targets up to the year 2006.

Q. Insofar as you were not self sufficient between 1975 and 1983, where were you buying your commercial factor VIII concentrate?

A. Yes, but this purchasing exercise was, as in England and Wales, the responsibility of local Health Authorities, Haemphiliac Centres, hospital pharmacists etc. We (the SNBTS) were not directly involved.

Q. Would you know where they bought from?

A. They would buy from the identical sources as our friends in England and Wales - primarily the United States of America, because, to the best of my knowledge, this was the primary source in those days.

Q. My note of your conversation with Ross referred to a managmeent report commissioned by the Department of Health which came out about a year after your article but which had been completed some six months before your article?

A. The published article we have just been talking about is not related to the Department of Health report to which you now refer.

Q. No, that's what I was going to ask: it was a separate article .....

A. Yes. Many years later, I wrote a BMJ leader which was a

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/a commentary of the state of the United Kingdom, but, in particular, the English and Welsh Blood Transfusion Services. In that article, I called upon a number of bodies, including professional bodies, to give assistance, because, in my view, the situation had deteriorated so much that there was now an urgent need to put things right. This is the paper which was published before the government management report appeared.

Q. Are we talking 1977/78?

A. No, 1987. If you have not read it, we are in some difficulty. It was my understanding that the Transfusion Centre Directors in England and Wales had persuaded the DHSS to establish a study on the future operational management of their services. At the time of my editorial, the DHSS management team had completed its studies and was, I believe, preparing its report.

Q. Now completed?

A. Yes. Perhaps the key section of my Editorial is as follows:-

"It is widely believed that its members were seriously concerned by many of their findings and recognize there is an urgent need for change. The only option that will provide the quality of service England and Wales needs, and one which will give the blood donors an assurance their gifts are appropriately used, is the creation of an integrated National Blood Transfusion Service which is removed from direct Regional Health Authority funding and managed by a new and separate Health Authority which includes the Blood Products Laboratory. This new organization must operate in the future beyond the reaches of Crown Immunity and be subject to the disciplines imposed by licensing authorities. It must have identified academic units committed to substantive research programmes, many of which would be designed to ensure that we compete effectively with industry in terms of product quality and availability. Above all, the overriding operational priority must be a commitment to provide blood and blood products to the NHS, based on patient need, and, in a cost effective manner ...."

I have been led to believe - but I have no evidence - that, as a result of my Editorial, this government report was delayed. It was eventually issued on the last day of Parliament, when it was prorogued for its Summer recess. It was simply announced that the report had been lodged in the House of Commons library. That was the summer of 1988. It was announced that there would be appointed a National Director for the NBTS in England and Wales. It is my understanding (but again I have no documentary proof) that government had originally no intention of establishing this post but that my Editorial had persuaded them to make some move towards an integrated national service. But I am afraid they have appointed a Field Marshall without an army. There seems

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/seems to me to be no effective management arrangements between the created NBTS Directorate and the RTCs.

Q. Can I read to you part of Graham Ross's note arising out of your telephone conversation with him on 28 November 1989 and ask you to say whether or not it accurately reflects your views:-

> "Appointed Medical Director of Scottish Blood Transfusion Service in 1979. At no time during the period he held that position did he make any offer to Elstree to process English or Welsh plasma nor was he involved, to his knowledge, in any discussions on that matter."
>
> Is that right?

A. Yes and no. As we began to develop our own self sufficiency programme in Scotland, some time in the early 1980's it became clear to us that our friends South of the Border were in serious difficulties and this had arisen because they had accepted that their laboratory at Elstree would be inspected. We understood it had been inspected and found to be in some difficulty. It became clear to us that, if we operated our facility 24 hours a day, 7 days a week, we could take some pressure off our friends in England. There would be two requirements: first, a modest expenditure on increased accommodation for what we call "finishing"(packaging and warehousing). Secondly, we required permission from the govenment to allow us to introduce a shift working system. We had been anxious to introduce such a system since our Centre had been commissioned in 1975 because the technology we had installed was quite unique. It had been designed to run 24 hours a day, 7 days a week with a computer looking after it. This unique fractionation system had been developed because, I believe, the design team had understood in the late 1960s, that, in addition to Scotland, we would be fractionating all the plasma from the whole of the north of England. They also believed this new technology would produce higher quality products at lower unit costs. This programme is now called continuous flow small volume mixing fractionation (CSVM) and, at that stage, its major proven advantage was in the area of large scale production of albumin. My predecessors had been very distressed when the final message came through that we would not be required to fractionate for the north of England but for Scotland only.

I can well remember the resultant disappointment of my then senior colleagues because it was thought sensible to have two major fractionation centres in the U.K. - primarily for strategic supply reasons and co-ordinated research and development. My predecessors decided they would not change the engineering system as such and so that potential capacity remained in place but all the associated "downstream" facilities - packaging etc were scaled down very substantially. When we came to the 1980s and were looking at our own plans for self sufficiency

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/sufficiency and, as our staff had gained confidence in running the CVSM system, we were keen to introduce a shift system. One way we thought we could get it was to offer our English friends some help because, at that time, they were in some difficulty. We did not offer to sell products - we hadn't enough plasma in 1981 for Scotland. What we offered was our fractionation capacity. I don't think we should delude ourselves that if it had come to pass it would have solved all the problems in England and Wales. Moreover, we didn't do the final sums and, at least initially, the assistance would have been directed towards albumin production only. We communicated our thinking to our employing authority, the Common Services Agency in Scotland. I was not, as far as I can recall, involved in direct communications with Elstree.

Q. And we are talking about 1981?

A. Yes, 1980/81. To the best of my knowledge our employing authority reported this to the Scottish Office and they reported it to the DHSS in London. I do not recall receiving any other response than one which suggested our albumin was below the standard required in England and Wales. On the other hand, what did happen soon after, and this may be totally coincidental, a Parliamentary Committee arrived here led by an M.P. from Sheffield. I believe he and all the members of this group were sponsored by ASTMS.

Q. Was that Norman Pettit?

A. No... Norman Pettit is the man, well the Pettit I am thinking of, who used to work at the Blood Products Laboratory at Elstree. The M.P.'s name was Flaherty or O'Flaherty. We were aware that the Union (ASTMS) had a closed shop at Elstree and the M.P.s wanted to talk about what went on at PFC and seemed to indicate that they had never heard of us!

We assumed at the time, but nothing was said, that this visit indicated that the Union was deeply concerned that there might be a movement of English plasma to Scotland into an environment which was not a closed shop. We assumed there was also understandable anxiety about jobs at Elstree and local union leaders had contacted the ASTMS sponsored M.P.'s requesting them to advise the Minister not to accept this Scottish offer. This is all assumption. All I can tell you is they came, they were very courteous, they had afternoon tea and went, but we got no subsequent feedback.

Q. Did you try to take it up again with your employing authority?

A. Yes, on several occasions, but, as I recall, they had had no clear response other than the comment made about the quality of the albumin product we produced, although this product has since been used in England on many occasions without ill effect. The issue seemed to simply run into the sand and, for

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/for whatever reasons, we got the distinct impression there was no enthusiasm from those colleagues responsible south of the Border.

Q. I diverted you by mentioning the name of Norman Pettit in an incorrect context. You obviously know of him. Who is he?

A. Norman is a personable individual who was, until recently, the sales manager or customs relations man for BPL. He has since resigned and joined the commercial sector. He is now European Sales Manager for Armour, a commercial plasma fractionation company.

Q. If the English authorities had taken up your offer to initiate a 24 hour shift working, would you have needed corresponding increase in your finishing facilities?

A. Yes.

Q. Assuming the money had not been made available for increased finishing facilities, would it have been possible to transport the fractionated product elsewhere, either to Elstree or perhaps abroad, for finishing - would that have been practicable?

A. I would need some expert advice on that. I would have thought that, if there had been an acceptance that we should actively explore this 24 hour period of fractionation, then the next requirement would have been to look very critically at the finishing problem. I should add that the offer made to our friends south of the Border was based on some reality. When we finally commissioned our Fractionation Centre we found we had a significant backlog of outdated plasma. We ran a day and night experiment on this backlog to see what was its operational feasibility in the context of producing albumin. We did our calculations at the end of the experiment (which lasted almost 3 weeks) and came to the conclusion that, running the Scottish system day and night, we could fractionate for albumin only the whole of the United Kingdom's then requirements in PFC. What we couldn't do was finish it. It is possible that the finishing could have been done elsewhere but this was not explored and it might have created difficulties for the control authorities in the context of good manufacturing practice - although these would have not been legally enforceable because both institutions had Crown Immunity.

Q. Ross has a note that when the Medical Inspectorate came to close down Elstree, it was no surprise to those in the Blood Transfusion Service on either side of the Border.

A. As far as I can recall, we were not surprised.

Q. Was it simply a question of totally outdated facilities, lack of capital investment or was there more to it?

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A. These inspections are rightly confidential and I therefore have no knowledge, but from our own experience faults would have been found not only in the accommodation but in working practices - good manufacturing practice. To the best of my knowledge, one of the problems for Elstree was in the period of say 1975 to 1980, the had not permitted the Medicines Inspectors to go into the place. They claimed Crown immunity - and therefore the inspectors had no right of entry. I should emphasise that BPL were within their legal rights to take this position and our experience would suggest that, if close down was threatened, then the major problem was more likely to have been accommodation deficiencies.

Q. He could close it down with a prohibition notice?

A. Correct, but only if they had not enjoyed Crown immunity. We, on the other hand, had always taken a different view. Despite having Crown immunity, we had welcomed the Inspectorate on the grounds that we would learn an immense amount about good manufacturing practice.

Q. I wonder if we can look at a different scenario and take as our starting point 1975 when Dr David Owen announced that he was going to allocated £5m towards the concept of self sufficiency.

A. I think you'll find it was £½m.

Q. Quite correct. England must have been alert, as their Scottish counterparts were, to the projected need for commercial concentrate for some time before?

A. I don't believe it would be appropriate to make that conclusion because England did not have similar co-ordinated management arrangements in place which made this type of forward planning possible. It was left to individual Regional Health Authorities to do their own thing. Scotland had a national co-ordinated service which was centrally funded and this enabled us to ask "What are we going to do over the next 10 years" and thereafter develop detailed and co-ordinated plans. I suspect an additional problem existed in England - even if they had generated increased plasma, I doubt the fractionation capacity required to fractionate the increase was available.

Q. An appropriate management mechanism was not in place in England?

A. Correct. The managerial infrastructure that could respond to Dr Owen's proposed investment was not in place in England.

Q. A total lack of meaningful infrastructure?

A. Yes.

Q. Who would be advising Dr Owen?

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A. I honestly don't know. There was a DHSS Blood Transfusion Service Advisory Committee. I sat on this Committee as an observer and, frankly, was frequently disappointed by the quality of its deliberations. I remember Dr Edward Harris, Deputy Chief Medical officer, chaired this committee, but I cannot remember whether it was funtioning in the late 1970s.

Q. Can we turn to the safety of imported American concentrate between the years 1975 and pre AIDS, 1982? It has been said to us by a virologist that this was dirty blood - a sewer of viruses. Was that a preception of American concentrate in the Scottish Transfusion Service over that period?

A. Yes, but this description is somewhat theatrical. I think we would simply say that, if you use paid donors as your source material and you are operating in any community in which that payment is important to the donor, then, when you come to ask serious questions about the donor's health and habits, the payment is an incentive to lie. This sort of incentive does not apply to the voluntary, unpaid donor. This danger was clearly seen by the WHO in 1975 in the context of the transmission of viruses in large pool plasma products.

In the period say between 1973 to 1980, several papers were published in medical journals describing the then new hepatitis test (HBV) used on blood donations. The prevalence for positivity reported in these papers was substantially higher in donations from paid donors compared to the unpaid. Even in America today if you compare the unpaid - v - the paid, it is still higher and this also applies to HIV and HCV detection.

Q. If we wanted to talk to an American, whom you respect and who could give us a potent insight into the sources of American commercial blood, is there anybody who comes readily to mind?

A. I would be in some difficulty because many of our American colleagues have been recipients of money from these Blood Companies and I am just not certain who they are. I have no evidence whatsoever that their British counterparts have taken money, but the Blood Companies have funded registrars' posts, research assistants, because my colleagues have not been able to get funds from goverment sources. In America I believe the position is somewhat different.

Q. If we look towards the World Health Organisation, is there anybody there who would help?

A. Not to my knowledge. WHO seems now to be totally committed to the development of Third World Transfusion Services. But the most important recent development comes from Brussels - the EC Directive 89/381.

Q. I would like to ask you what you see as the primary dangers to the plaintiffs' case in this litigation?

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A. I think there are two related things. One is I have always been consistently disappointed that the Haemophilia Society did not, in this crucial period, mount a major campaign - a really sophisticated media campaign - to seek support for the NHS factor VIII producers. Nor did they, to the best of my knowledge, make any constructive contact with any of the NHS producers. Certainly I can say that they made no contact with us. Our contact with the Haemophilia Society is of only two to three years' duration.

The second thing is more sinister. There is an organisation called The World Federation of Haemophilia, an international organisation established to represent patient interests.. Many years ago I joined but resigned within a year after a meeting in New York. I formed the opinion that, at that time, this organisation was heavily financed by the commercial plasma fractionators. At the New York meeting I talked, in confidence, to some of the British delegates about my concern and asked whether the British Haemophilia Society and/or individual members were the recipients of money from these commercial organisations. I could not get a straight answer and was convinced that at that time it was almost certain this was so. Some of the individuals I spoke to in New York are now deceased (with AIDS) and I suspect their relatives may be found in your group of plaintiffs.

Q. It has been suggested that blood originating in most Third World countries or from paid donors is always at higher risk of transmitting viral infection, no matter what the nature of the screening process; is that something you would agree with or not?

A. Yes.

Q. And this risk had long been recognized?

A. Yes.

GRO-C: John D Cash

GRO-C 29/11/90.