Archer Inquiry

Written submission of Dr Mark Winter

I am Director of the Kent Comprehensive Haemophilia Care Centre in Canterbury, and took up my post there in December 1983. I am therefore a member of the UKHCDO Executive Committee and serve on a number of their working parties. I have for a number of years been the DOH appointed Medical Trustee for the Macfarlane Trust. I was also the founding Medical Chairman of the Haemophilia Alliance, an organisation that brings together Haemophilia health care professionals and people with Haemophilia; the Alliance has worked together over the past few years to set formal commissioning standards for people with hereditary bleeding disorders. As far as I am aware, I am now the only Comprehensive Care Centre Director in England who was around during this critical period prior to 1985 and who is still working. I am here in a personal capacity todat and am not representing any of the above organisations.

I have chosen to give evidence because I support the purposes of the inquiry, although I wish that it had taken place fifteen years ago. This is the worst medical disaster in the history of the NHS and it is right and proper that an inquiry should be held.

I am not able to make any detailed comments about the political initiatives of the 1970s towards self-sufficiency since I was only a Haematology Registrar at that time. I am also not able to make comments about decisions taken by those responsible for the regulation of medicines such as factor VIII, both in this country and in the US, since I have no expertise or experience in this area.

What I can do is to try and describe as a doctor what it was like to look after patients during the time when HIV infection was occurring and to make some reflections on the events that occurred in those times. I have considered it most helpful to divide my comments into three areas:

- Spring 1984, when the HIV epidemic was evolving and doctors were trying to make choices about the type of treatment that patients with Haemophilia should receive in the light of this evolving evidence
- Autumn 1984, when the HIV test had become available and doctors were trying to decide whether those patients who had tested positive for the new virus should be told, and what the significance of a positive result meant.
- The subsequent clinical course of patients who were infected with HIV and Hepatitis C.

Spring 1984

Haemophilia is a life long and severe hereditary bleeding disorder characterised by spontaneous bleeding into joints and muscles. Without treatment we know that life expectancy is very limited. The Birch report in the 1930s disclosed that only 20% of patients with severe Haemophilia could expect to live beyond twenty years. A Finnish study in 1960 showed that the average life expectancy for patients with severe Haemophilia was twenty five years. The commonest cause of death was internal bleeding, particularly into the brain or gastro intestinal tract. Although Haemophilia appears to have been around for a very long time, no treatment was available until the early 1960s because factor VIII circulates in the blood in only tiny amounts and no

way had been found of concentrating factor VIII from blood.

Concentrates of factor VIII and factor IX eventually became available in the early 1970s and were a revelation in that for the first time patients with Haemophilia were able to gain control over their lives. Children could start going to normal schools and home therapy programmes were initiated as the concentrates could be stored in a domestic refrigerator. Episodes of acute bleeding could be treated promptly and dental and surgical procedures could be managed without any great problem. Patients were able to regain a sense of normality in their lives and the background fear of intracerebral bleeding diminished. This period, for a few years from 1974, became known in retrospect as the golden interval, a time when at last the outlook for patients with Haemophilia appeared to be very promising(although there was a major episode of ?hep B in ?Bournemouth with fatalities in 1976 – deaths from acute hepatitis were in mild haemophilacs when first treated with conc and got ?hep B).

Very shortly after the introduction of these concentrates, it became apparent that nearly all regularly treated patients displayed biochemical abnormalities of liver function of a type that would be compatible with a form of Hepatitis virus. As only a few of these patients had either Hepatitis A or Hepatitis B, it was assumed that these patients might prove to have a third Hepatitis virus, named as non-A, non-B Hepatitis (subsequently identified as Hepatitis C in 1989). However, these patients remained clinically very well despite their biochemical abnormalities of liver function, which were not held at that time to be of particular significance.

During the 1970s there was an appreciation amongst the Haemophilia community of the sourcing of the various concentrates and this awareness extended to patients as well. There was a perception that US derived factor VIII and factor IX, being derived as they were from commercial donations, were far more likely to carry viruses (and possibly different viruses than UK) than factor VIII and factor IX that had been made from UK plasma, where donations were voluntary. A number of patients would refuse to receive concentrate that was of US origin. It was for this reason that representation was made by the Haemophilia community to the DOH that there should be self sufficiency in blood products.

In the summer of 1982, the first patients with Haemophilia were described as having AIDS in the US. In January 1983 the risk to patients with Haemophilia was becoming more apparent and an editorial in the New England Journal of Medicine recommended the use of cryoprecipitate rather than concentrate. Despite this, there was great reluctance among both the medical and patient communities to consider a move away from concentrates. This was mostly because of the very significant advances in general health that had followed the introduction of concentrates and also because of doubts to the validity of the new data. At this time, the commonest cause of death was still cerebral haemorrhage (my recollection is that there were 10 deaths from cerebral bleeds in 1983 in the UK and only a handful of AIDS cases world wide)and doctors were very concerned not to withdraw concentrate from their patients. Parallel with this, in May 1983 the Haemophilia Society asked the DOH not to restrict the importation of US factor VIII and IX.

In the same month, at a meeting of the Haemophilia Reference Centre Directors, it was minuted that 'there is insufficient information to warrant changing the type of concentrate used in any particular patient' and 'it was agreed that there was, as yet, insufficient evidence to warrant restriction of the use of imported concentrate in view of the immense benefits of therapy' In june 1983 recommendations were issued by Reference Centre Directors rather than Hepatitis working Party?(below).

In July 1983, as further cases of AIDS amongst the Haemophilia population in the US were becoming apparent, the Hepatitis Working Party of UKHCDO recommended that cryoprecipitate should be used in preference to concentrate for the treatment of children under four years of age, for new patients with Haemophilia and for mildly affected patients. They also recommended wherever possible the use of Desmopressin (DDAVP) a drug that raises factor VIII levels in patients with mild Haemophilia. However, in the same month, the Committee for Safety of Medicines stated that they did not believe that there was a sufficient supply of cryoprecipitate for patients with Haemophilia, if there were to be a switch away from concentrate.

In November 1983, the health minister Kenneth Clark announced in Parliament that "there was no evidence that AIDS is transmitted by blood products".

At the annual general meeting of the UKHCDO in December 1983 in Oxford, Dr Chisholm from Southampton asked whether there should be a switch to cryoprecipitate. The minutes state that 'Professor Bloom (from Cardiff) replied that he felt there was no need for patients to stop using the commercial concentrates because at present there was no proof that the commercial concentrates were the cause of AIDS...after discussion, it was agreed that patients should not be encouraged to go over to cryoprecipitate for home therapy but should continue to receive the NHS or commercial concentrates in the usual way'.I do not think there would have been the manufacturing capacity to move over to cryo for everyone and the experience in the US was that even where this was recommended the patients did not wish to change. Some US evidence that even those treated exclusively with cryo had a high risk of HIV

In retrospect, there are a number of factors which can be seen to have lead to the stance that was taken by Haemophilia Centre Directors at that time. Beyond the unwillingness to retreat from the very significant and recent therapeutic advances offered by concentrate, it is important to note that – unlike today – there was at that time no overarching advisory body with a remit for the new virus (then known as HTLV-3). The government's Expert Advisory Group on AIDS was not convened until early 1985. Today, for instance, we have very substantial advice from the variant CJD Working Party which advises Haemophilia doctors at all times in relation to variant CJD In 1997 despite there being SEAC it was UKHCDO that first questioned publically the safety of UK plasma and came under a lot of pressure for having 'gone over the top'. No such national advice was available to Haemophilia doctors in 1983 concerning HTLV-3. UKHCDO had established an ad hoc arrangement with Dr John Craske, a virologist in Manchester, and he was the only virologist, as I recall, to whom advice was obtained concerning the evolving HIV epidemic. In turn, this was a reflection that the science of virology itself was very poorly developed at that time and existed in Pathology departments as a sub-division of Microbiology. There were very few hospital virologists.

There was in any case, as can be seen, no consensus among Haemophilia doctors as to the importance of the evolving epidemic at that time and - beyond the recommendations concerning the use of cryoprecipitate in selected groups - there was therefore no standardised advice (see above letter issued by Bloom and Rizza on 24th June to all haemophilia centres)issued from the UKHCDO to inform Haemophilia doctors around the country as to how to address the various issues that were evolving.

By early 1984 a number of commercial companies had begun to work with heat - treated concentrates, based on the observation that heat-treatment might theoretically inactivate viruses present in the concentrates. In February 1984 Alpha Therapeutics obtained a licence in the US for their heat-treated product and shortly afterwards

Professor Savidge (from St Thomas' Hospital) and I began discussion with the company about whether we could possibly use this product on a named patient basis for our patients with Haemophilia. This was a reflection of our increasing concern about the data emanating from the U.S. This new product was 50% more expensive than the current unheated product ?Mention that there was no evidence that heat treatment would inactivate possible infectious agent and there was a real possibility that heat treat might denature VIII giving rise to new epitopes and inhibitors which might render patients unresponsive to further VIII therapy.

The decision as to whether one would recommend the use of heat treated factor VIII to a patient rather than the currently available non heat-treated factor VIII was particularly difficult, especially as the former was of US origin (and therefore from paid donors) whereas the latter was of UK origin (and therefore from voluntary donors). There was again no consensus among Haemophilia doctors as to what the preferred product at that time should be and there were a number of senior Haemophilia doctors who continued to express the view that UK plasma was safe and that HIV infection would never happen if patients were exclusively treated with factor VIII derived from UK plasma. This was supported by the lack of any clinical cases of AIDS amongst patients treated exclusively with UK plasma at that time also a lack of evidence of AIDS cases in Germany which used a lot of US concentrate so it was not universally agreed that US concentrate necessarily carried a higher AIDS risk.

Professor Savidge and I decided that there was compelling evidence that currently available concentrates not only transmitted non-A, non-B Hepatitis (subsequently known as hepatitis C) but were also very likely to contain the new virus (then known as HTLV-3).

In May 1984 therefore I approached a small number of patients who required major surgery or suffered acute trauma and who had had little or no factor VIII treatment in the past. I offered them the choice between these two concentrates. The choice was stark – on the one hand, the currently available licensed concentrate (unheated) from voluntary donors which seemed to definitely transmit Hepatitis C and possibly also HIV and on the other hand the choice of a newly available (albeit unlicensed) concentrate from commercial donors which on theoretical grounds might prove not to transmit either of the viruses. These theoretical premises turned out to be correct transmit HIV How many of the patients treated with the Alpha product did not get HIV – I think this has been published – ?several years later , perhaps should mention that it did not prevent NANB hepatitis.Was this use in agreement with the advice of Bloom and Rizza to put patients into studies and not on a named patient basis 24th June 1983 This was one of those thankfully rare occasions in medicine when the advice you gave to a patient could either save his life or end it – one of the patients treated by me with heat treated factor VIII at this time had never received factor VIII before but was subsequently given non heat-treated factor VIII in another centre, acquired HIV infection, passed it on to his wife, and subsequently died.

From 1st July 1984, only heat-treated factor VIII and factor IX was used exclusively in our centre.

Autumn 1984

In the latter part of 1984 there was still great confusion and bewilderment about the evolving epidemic and no consensus as to the clinical management of patients. In November 1984, for instance, Dr Craske wrote to Haemophilia doctors, making a

number of statements:

- that only a proportion of patients transfused with an infected batch were likely to contract HIV
- that it was likely that the proportion of patients who contracted HIV and subsequently AIDS would be of the order of 1:100 to 1:500
- that the long term prognosis for patients with HIV was unknown
- that there was evidence that HIV infection could be transmitted by sexual contact
- that it was not possible to distinguish those patients who were likely to transmit HV by means of laboratory tests

As can be seen, some of these statements proved to be accurate, others very much less so.

In the summer of 1984 HIV was isolated for the first time and by August of that year a blood test (then known as HTLV-3 antibody) had become available in the UK in the laboratory of Dr Richard Tedder at University College Hospital. UKHCDO arranged for all samples from patients with Haemophilia who might have been exposed to HIV to be forwarded for testing to Dr Tedder's laboratory.

From the time when it had been first established that Hepatitis viruses were likely to be present in factor VIII concentrates in the mid-1970s – I think before this date, Haemophilia doctors had regarded it as their responsibility to regularly monitor their patients for the presence of new virus infections. When the HTLV-3 antibody test became available therefore – and in the absence of any standardised advice – there was again a diversity of practice amongst centres as to the way they handled the situation. In our centre, we informed patients that a blood test was now available and that their blood was being sent to UCH for testing. In some other centres, they saw the availability of the new test as merely an extension of their pre-existing screening programme and did not perceive any need to inform patients. AIDS testing was being carried out in a similar way, and on a larger scale, by Infectious Disease specialists working in AIDS treatment centres. For instance Professor Ian Weller of the Middlesex Hospital – one of the major AIDS centres in London - was quoted as saying " we performed a large number of HTLV-3 tests without written consent. Blood was taken from patients with AIDS, patients with lymphadenopathy... and controls" (quoted in "The End of Innocence" by Simon Garfield, page 55)

Although, twenty five years later, this may today seem shocking (why shocking? – people were dying and there was an urgent need to get on top of the epidemiology – it was only much later that the implication of testing became apparent) it was very much the culture of medicine at that time but also the scale of the unfolding uncertainty . It was for instance a common practice then to withhold a diagnosis of cancer from a patient, with only the relatives being informed.

In 1984, there was of course no concept of pre-test counselling - this concept only emerged years later as a result of the HIV epidemic and the impact that a positive test had on a patient's life style including the possibility of not obtaining life insurance and mortgages.

In November 1984, I received the results of the thirty or so patient samples that I had sent to Dr Tedder's laboratory. These showed that in all but one case, the patients were positive for the new virus. Eighteen of these patients were children.

What did the phrase 'HTLV-3 antibody" mean? Antibodies to some viruses such as chickenpox, measles and mumps are associated with immunity whereas

antibody to other viruses, such as Hepatitis viruses, can be associated with active infection. Did these results therefore mean that the patient had been exposed to HIV and was immune or did the results mean that the patient had active HIV infection? The latter turned out to be true but at that time nobody knew. It was not only Haemophilia doctors who did not know what to say. Professor Weller was telling his patients at the Middlesex 'we don't know what this test means...it may well mean that you have been infected with the virus and have recovered...you've got antibodies and you may be immune' (The End of Innocence, page 55).

It was therefore very difficult what to work out to say to patients without unduly alarming them. In our centre, I told each of the patients that they had tested positive for the new virus and I advised them about the possibility of transmission through sexual activity. I told them that we did not know what the result meant but that we would be monitoring them very closely including regular assessment of their immune function.

There was again lack of consensus, and a lack of standardised advice, concerning whether patients should be told their results or not and this lead to differing practices in centres across the country. In Dr Craske's letter of November 1984, for instance, he advises Haemophilia doctors that they have two choices, of either telling the patient or not. Although on balance he recommends that the patient should be told he concludes 'ideally I think he should, but this will depend on many factors including the amount of anxiety concerning AIDS there is already present at the centre, and the degree to which the patient is capable of understanding the situation. An alternative might be to inform the patient's spouse or other close relative as is done when patients develop malignant disease. This will be at the discretion of the local Haemophilia centre director'.

In the following month, at the UKHCDO Reference Centre Directors meeting of 10 December, it is minuted that 'patients who ask their HTLV-3 antibody results should be informed of them, otherwise it is up individual directors to decide whether or not they wish to tell their patients'. An Advisory document issued 14th December 1984 gave reasonably explicit advice

In addition to the lack of standardised advice as to how to approach the epidemic that was evolving amongst Haemophilia patients, there were a number of other factors which affected the way in which doctors responded to the evolving crisis. I have already commented on the difficulty of obtaining virological (but no one knew for certainty about significance of anti-HTLV positivity except that in some people it reflected exposure to the virus that probably casued AIDS but there was a lot of uncertainty about the false positivity rate – this was one of the reasons for delay in rolling it out to blood transfusion centres for screening donations advice. A further point of particular importance is that most of the senior Haemophilia centre directors at that time were not clinically trained some may have had different training from us but I think the majority were clinically good, knew their patients very well and they understood the dilemmas of the evolving situation. Traditionally, Haemophilia doctors had worked in laboratory medicine and often had scientific and academic backgrounds. There was no tradition of clinical training in haematology until the mid-1970s. As a result, many of the senior doctors trying to respond to the evolving crisis in 1984 had little or no experience of telling patients bad news, of dealing with very sick and dying people and of discussing possible sexual transmission of a virus.

When I began Haematology training in 1976 I was one of the first registrars who had done general medicine and who had obtained the Membership of the Royal

College of Physicians. From that time onwards, clinical training and MRCP became mandatory for all Haematologists.

The years from 1984 onwards were the very darkest of times, as patients began to die. Many of these patients were severely disabled with Haemophilia and spent their life in wheelchairs, as they died of AIDS. There was no antiretroviral treatment until the late 1980s but there was pentamidine and later septrin and all that could be done was to treat symptoms as best one could and to be there as not only a doctor but also a confidante and companion unto death. There was intense stigma surrounding the virus and patients often felt unable to discuss their illness with their family and friends. Many overt acts of discrimination were carried out against these patients at this time because of irrational fears about the AIDS virus and the way it could or could not be transmitted.

There were particularly difficult problems concerning the management of children. All of the schools where our children attended wanted the children to leave the school because of fears of transmission of the virus to other children in the school setting. At the parents request I told all of the children individually, usually in the school holidays and at times when they were still relatively well.

We spoke too of the 'double guilt' of the mothers of these children for not only had they inadvertently passed on the Haemophilia gene to their son but they had also been likely to have injected the contaminated batch of factor VIII as part of a home therapy programme. These women needed very intensive support and counselling

Clinical features of HIV and Hepatitis C infections

There are important differences concerning the way in which HIV and Hepatitis C were acquired by patients with haemophilia.

As mentioned earlier, it was apparent at a very early time following the introduction of commercial concentrates and I think NHS in the early 1970s that these products were likely to transmit the virus that subsequently became known as Hepatitis C. Published papers at that time indicate that the incidence of Hepatitis C infection in US donor plasma was around 3%. Given that batches of factor VIII concentrate were derived from around 20,000 donors, one could conclude that a patient with Haemophilia receiving a treatment with US factor VIII at that time was likely to have acquired several hundred different Hepatitis C infections. Many of these patients would have been receiving up to three treatments each week

Although the incidence of Hepatitis C in UK plasma at the same time was much less, a critical observation is that it was still of the order of 0.5-1.5%, as reported in two studies in the early 1980s.

One can conclude from this data that if the political initiatives towards self-sufficiency had been achieved, in 1976/1977 for instance, that for most (but not all) patients with Haemophilia they would still have been very likely to have acquired Hepatitis C infection from UK derived concentrates at that time.

One can therefore say that most episodes of Hepatitis C infection could not have been prevented in patients with Haemophilia, certainly not in those who were regularly treated. There is a relatively small number of patients with mild Haemophilia (who could have been treated with DDAVP) or who had treatment in the early 1980s (when heat-treatment was becoming available) but beyond this nearly all patients would have been infected with Hepatitis C even if the UK had been self-sufficient by 1977.

With HIV, the situation is very different. A particularly important study was carried out by Dr Peter Kernoff at the Royal Free Hospital in the early 1980s. It was Dr Kernoff's practice to freeze plasma samples on his patients. When HIV testing became available in 1984 therefore he was able to identify around 100 patients with HIV in his centre and to retrospectively test their blood to try and identify how long their HIV infection had been present. That data indicates that most patients had had HIV in their blood for several years prior to 1984. However, no patient samplewas identified prior to 1980 as being HIV antibody positive.

The clear implication of this very important study is that the introduction of self-sufficiency, in 1977 for instance, would have been likely to have had a significant impact on the number of patients who subsequently acquired HIV this is speculation – would probably have been less but may be not a lot less. You may recall Australia being self sufficient in blood products but it ended up with a high HIV rate in haemophiliacs. As you know in Scotland a single batch infected about 17 patients and it is possible that there was only a single HIV positive donation into this batch. At this time there were no clinical cases of AIDS in Scotland and with its stable population it is my opinion that it HIV risk from plasma pools would have been less than plasma pools in England – I therefore think that NHS concentrate in England would be mid 1984 have had a significant risk of transmitting HIV. Glasgow produce some evidence that that ?16% haemophilacs treated exclusively with NHS products got HIV compared to 35% who received commercial (published December 1984 ?BMJ). The HIV incidence for IX deficiency which was predominantly treated with UK factor IX concentrate was lower but this may well have been due to some virus exclusion in the manufacturing process

In parallel with this, one can look at the situation in Scotland which was more or less self-sufficient in factor VIII and factor IX concentrates. When HIV testing became available, it was apparent that there were hardly any cases of HIV in Scotland, in support of the above comments.

HIV and Hepatitis C have different symptomatology. Most patients with HIV develop symptoms of ill health at a fairly early stage of the infection, including weight loss, night sweats, loss of appetite, lymphadenopathy (swollen lymph glands) and candida (thrush). In contrast, as the inquiry has already heard, many (but not all) patients with Hepatitis C could be relatively asymptomatic for a number of years whilst some may have long term symptoms of tiredness, nausea and abdominal pain.

The latest Macfarlane Trust data indicates that only 366 out of 1,246 original registrants (29.4%) remain alive. According to annual returns reported to the UKHCDO secretariat by all Haemophilia treatment centres, the number of liver deaths over the past 20 years has been less than 100 Given that around 4,000 patients are known to have been infected with Hepatitis C, this will give an overall mortality of around 2-3% in contrast to the very high mortality seen with HIV infection.

Many patients acquired both HIV and hepatitis C and this is currently leading to very significant problems in their management. The management of HIV infection has become much more advanced of late and thankfully many patients with HIV now have unmeasurable HIV loads and have been able to regain a good quality of life and indeed return to work although this treatment does involve long term medication with a combination of antiretroviral drugs which can have ide effects.

Therapy of Hepatitis C is less successful in those patients who also have HIV and nearly all deaths in the Macfarlane Trust community over the past few years have been due to liver disease. We urgently need therefore better drugs in the management

of Hepatitis C when patients are also co-infected with HIV.

There are also concerns about the long term prognosis of patients with Hepatitis C in those who have not been co-infected. Recent evidence suggests that the rate of cirrhosis can increase after thirty years of infection as can the occurrence of a rare type of liver cancer known as hepatoma. For these reasons, Haemophilia doctors are particularly active in trying to eradicate to treat hepatitis C infection in their Haemophilia patients.

I have been a Trustee of the Macfarlane Trust for a number of years and understand well the issues currently being faced by those who have survived. These people have been living with not only Haemophilia (a very painful lifelong disorder) but also HIV and Hepatitis for more than twenty five years. The obvious phrase to use is that everything is worn out – their spirits, their emotions, their relationships, their finances. These people continue to need the very best of support in helping them to come to terms with the terrible medical disasters that have befallen them.

The events that I have been describing happened nearly twenty five years ago. In retrospect, one can accept that there were a number of deficiencies in the way in which some patients were managed - in the way in which their original HIV test was carried out, the way in which the results were or were not transmitted, and the way in which their care was subsequently given. I have tried in this submission to identify some of the causes that underlay this variability of care. In looking back at this time it is unreasonable to apply the standards of today to the early 1980's. Things were very different then; in particular, medicine was more paternalistic. Might be useful to put in some degree of international comparisons – ie this was a 'worldwide 'problem and the UK was a leader in investigating hepatitis in a structured way, was an early proposer of heat treatment etc

I would wish to conclude by strongly supporting my medical colleagues of the time, many of whom have since died. As doctors, we no longer take the Hippocratic oath but the principle remains the same. 'Primum non nocere' - firstly do no harm. Although it was not discussed very openly amongst us, there was a great sense of shock and bewilderment as to what was happening. Haemophilia care is lifelong and many of the patients who were infected and died had been looked after for many years by these doctors and nurses.

I have been a witness to the suffering of many patients with Haemophilia who were infected with viruses through their treatment on the NHS. Nothing can undo the way in which their lives have been ruined though for some this inquiry may help.

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