THE PENROSE INQUIRY

WITNESS STATEMENT – PROFESSOR CHARLES FORBES

1. My interests in haemophilia started in 1961 when on qualification I started at the Royal Hospital for Sick Children in Glasgow. One of the duties in this surgical position was to look after the children with haemophilia who had developed surgical problems, especially joint disease.

2. After various positions I took the opportunity of secondment to the University of East Africa (Kenyatta National Hospital). This secondment was in association with Professor A S Douglas who was at the Royal Infirmary in Glasgow at this time and had been seconded also for one year. He was an acknowledged expert in the care of patients with haemophilia and indeed had originally separated haemophiliacs into type A and type B.

3. Professor Douglas' work started in Oxford in the Haemophilia Centre run by Professor R J McFarlane. He was responsible for the differentiation of haemophilia into two separate types - classic haemophilia and Christmas disease. In Glasgow he had documented most of the patients in the West of Scotland and had been responsible for setting up the Haemophilia Centre there. He was involved in the general treatment of adult patients (children were treated separately at the Royal Hospital for Sick Children by the then Director Professor Michael Willoughby – now deceased).

4. At the end of the period of secondment I was asked to go to work at the Royal Infirmary with a special job in the care of patients with haemophilia and related bleeding disorders. I stayed there until 1968 when I took the opportunity of a further period of higher training in Cleveland, Ohio with Professor Oscar Ratnoff. Professor Ratnoff was an international authority in coagulation disorders and had made many of the seminal discoveries on a whole range of different bleeding disorders. It was my opportunity of working with him and his team. I was responsible for the purification of Factor XI and the definition of its properties. In the clinical area we were responsible for consulting in various bleeding patients as they came into the hospital.

5. In 1971 I returned to the Royal Infirmary in Glasgow to take up a position in medicine, under the direction of Professor A S Douglas who was the Consultant, but with special reference to care of patients with haemophilia and related coagulation disorders. The general duties of this position were to look after the various problems in haemophilia. It provided me with vast experience of management of such patients and their families.

6. The West of Scotland Haemophilia Centre became one of the largest in the country with approximately 300 active patients. We managed these mainly on an outpatient basis with a daily morning clinic for particular bleeding problems and for advice and diagnosis. I was responsible for the front line management of these patients on a daily basis including a commitment on call every weekend. This was an immensely good opportunity for seeing a range

of obscure bleeding problems. I am not aware of seeing the World in Action programme in December 1975 and indeed did not watch much television at that time but I was not aware so it had no effect at all on use of concentrates. In any case we were extremely limited at that time by what was available through the Scottish National Blood Transfusion Service.

7. The seminar 'Unresolved Problems in Haemophilia' was an educational seminar held in Glasgow in October 1980 to try and resolve some of the problems that had arisen over the few years prior. There was no payment to individuals and the programme was chosen by myself. The speakers no doubt got travel expenses but as far as I am aware there was no direct payment of any kind and certainly not to ourselves.

8. All seemed well and straightforward until I received a phone call some time in 1980 from Professor Ratnoff (Cleveland, Ohio) who was enquiring if I had seen any unusual types of haemophilia in which patients were clearly ill with various opportunistic infections and tumours. I believe that 1980 was the date when I got this phone call from Oscar Ratnoff as he was talking about things I had never heard of and clearly at the end of the day this was the start of AIDS in Haemophilia in the USA. I had not seen anything like that but this was to be the start of the epidemic of AIDS.

9. The area of research in Glasgow in which we were then involved with was to look at immunity in patients with haemophilia. It was quite apparent that there was an association between the administration of large amounts of

Factor VIII concentrate and the immune process which was suppressed in many patients. A variety of other investigators were finding the same kind of abnormalities using a range of biochemical tests and the real question was what did this mean? Was there something in the Factor VIII or IX concentrates that did suppress these tests of immunity and what did this really mean in terms of the long term care of patients?

10. Subsequently it became apparent that plasma concentrates of all types could be contaminated with a virus which was subsequently known as HTLV III and later as HIV. This was meant to be a global statement of the next few years probably 5 years from 1983 when it was apparent that other types of concentrates could transmit the virus. For a long time after the initial cases of AIDS was reported there was great debate about the best way of treating bleeding. It was certainly not possible to stop the use of concentrate as bleeding would have resulted in death and the general reaction of most Haemophilia Directors at that time was to continuing to treat the bleeding with concentrate. It was speculated by us that something in the concentrates suppressed the immune system of recipient patients and that this made them more likely to be infected by the virus which was then appearing in concentrates.

11. The subsequent history is well set out in Chapter 8 of the Penrose Inquiry Preliminary Report which sets out the progression of the disease from the first recorded patients in all the risk categories and especially in haemophilia. In 1982 the first documented cases of patients with haemophilia

with AIDS were recorded and that the progression of the disease and the range of symptomatology was typical of other patients in other risk groups eg homosexuals, drug abusers etc with the same kind of outcome of 50% mortality.

12. Prior to this it is worthwhile noting that, in retrospect, other patients who probably had AIDS had been recorded intermittently and sporadically in the general medical literature. The "first" report of AIDS in haemophilia was in 1982 (16 July) in MMWR and subsequently in patients receiving blood transfusion. These were heterosexual males and would not be associated with the other reports which had been in other risk groups i.e. homosexual males and intravenous drug abusers. The reported incidences in the third group i.e. people from Haiti has never been satisfactorily resolved.

13. This report in MMWR was the first report of transmission in blood products. In the following months there was a lot of discussion about whether blood products should be stopped in terms of treating haemophiliacs. The general advice at that time clearly was that there was more danger of death from bleeding than from any disease that might be transmitted. There was much disagreement about whether this transmission was of a virus or some other agent within blood products. This remained a difficulty for many months and the general consensus was that treatment should continue if there was life threatening bleeding as that was going to be the only way to stop it.

14. Over the months to come it became clear that AIDS was not limited to the United States of America but was now present in the UK with small numbers of patients being diagnosed. However as yet there was no consensus that this was due to a virus or whether there was some immune problem which then led to the disease. In the group that believed that this was an infectious agent that was transmitted in blood products there was a movement away from the more potent concentrates some of which were imported and some of which were made by the NHS. The thinking being that the more donors that had been pooled together the more likely the chance of an infectious agent being transmitted. We in the West of Scotland continued to use cryoprecipitate for both routine treatment in the Centre but also in the distribution to people on home therapy. This was not nearly as efficient and as effective as the use of a safe concentrate but that was the situation at that time.

Specific questions in request for a witness statement

15. In 2 (iv) the suggestion is that there had been no representation of Scottish centres at this meeting. As I indicated I have no recollection of being at this meeting but I certainly attended many others about that time but you may have obtained minutes of the meeting in which case my name would be either there or not there. That is not my personal recollection but I have no papers now as I destroyed all my records when I retired. I don't think at any time we, in Scotland, felt that we were isolated from the rest of the UK and we

always felt that we were part of the universal policy which was thrashed out at the national meetings.

16. In 2 (vi) I do not remember the meeting where Dr Galbraith is said to have recommended that blood products from the USA not be used. We would never have been in agreement as the risk of death from bleeding was always much greater.

17. At paragraph (vii) there is a suggestion that England and Scotland had different views and that information was not transmitted to Scotland. I don't think that is true and it is certainly not my recollection. We worked closely with the English directors and the Welsh and Northern Ireland groups and I think that we had a concerted common policy. Great debate occurred every time the groups met. The question of not using concentrates was debated many times but the argument that the chances of death were higher from bleeding than from use of concentrate or related materials always carried the day. Concentrate continued to be used and to be imported.

18. We looked very hard for alternatives for people who rarely needed concentrate and especially children. Consequently, mildly affected patients were usually given cryoprecipitate from a small pool of donors which we considered safer. As children required smaller amounts of concentrate or Factor VIII in whatever preparation they should be given cryoprecipitate from a small pool.

19. There has been a suggestion in various comments about DDAVP. This is a non plasma derived pharmaceutical which does not have any contact with blood products but which does stimulate the release of small amounts of Factor VIII from blood stores. It is not without its own problems and we published some information of the major disadvantages of use of DDAVP. It could not therefore be used routinely.

20. See reference (from GDO Lowe). Lowe G, Pettigrew A, Middleton S, Forbes CD. The title was DDAVP in Haemophilia and was in Lancet 2 1977 page 6144.

21. With regard to viii you ask about the attendance at WFH and ISTH meetings at the Karolinska in June 1983. I think, from memory, only that I was there and it was a forum to discuss the problems that we were all now seeing in Europe with regard to AIDS transmission and related syndromes. These meetings were helpful in spreading information around centres.

22. In ix you ask about a meeting of the biological sub-committee. I don't know if there was any representation at this meeting from others in Scotland but I wasn't there.

23. At 3 you ask about the meeting in Aarhus on 19-21 October and also the subsequent meeting of the UK Haemophilia Centre Directors in Manchester and the subsequent WHO conference in Geneva on 22-25 November 1983. I don't know the answer to who from Scotland attended. I

am not sure it is correct to say that the emphasis was on maintaining the use of commercial concentrates. We certainly had made an effort to provide cryoprecipitate from small pools for mildly affected patients and even those who were on home therapy. This may be the reason that when we eventually had a test for HIV that only 16% of our treated patients tested positive. The figure of 16% was arrived at by direct observation and measurement of stored samples in our possession at that time and was measured by standard assay which had become available. This was published in Lancet 1 pages 524, 525 1985. The second reference that might of value is Lancet 2 1444-1446 1984. I must say that we always felt that we were deprived if we could not give concentrates which were more effective and more efficient.

24. Compared to other large Centres in England where concentrates were widely used they had up to 90% of their severe patients HIV positive compared to only 16% of ours. So at the end of the day we were very lucky.

25. With regard to 3(iv) I would make the point that we all felt that it was good clinical practice to avoid the use of blood and blood products unless there was very good reason.

26. Commenting on 3(v) I don't know what evidence or where this came from but we have not been aware of patients attending GU clinics (especially haemophiliacs) who would always be referred on and I actually don't believe it either!

27. Now to 4 although you have said that Scotland was self sufficient in terms of Factor VIII concentrate and Factor IX concentrate I don't think it ever really was. We always had difficulty getting sufficient concentrate to treat patients and as indicated we continued on small restricted pools of cryoprecipitate which we thought were never as effective or sufficient. We never had a separate budget for commercial concentrates although I know that some other English centres did.

28. With regard to the statement on the use of heat treated concentrate (4) I think most of us were pretty sceptical. We believed that the Factor VIII activity would be destroyed on heat treatment. However, many experiments were carried out and in 1984/1985 such products did become available although some of them were pretty insoluble and therefore ineffective. In the experiments it became clear that at least one commercial concentrate was known still to transmit HIV infection despite being heat treated. This led in the longer term to a longer heat treatment period and also a higher temperature at which the product was heated. Heat treatment therefore was of great value at that time in removing the infectivity of the virus.

29. I think that the attention and the anxiety and distress associated with HIV infection made us take our attention from the equally important and in retrospect perhaps a more important aspect of other infection which was Hepatitis C and it is now clear that Hepatitis C has caused a further number of deaths from liver disease and liver failure. I have had the unique experience of looking back at this episode (I left in 1987) and it is apparent that Hepatitis

C in the long term has become a much more serious and sinister disease with many fatalities.