MERSEY AND NORTH WALES REGIONAL TRANSFUSION SERVICE

RESPONSE TO QUESTIONNAIRE HIV LITIGATION UPDATE

NOVEMBER 1989

Paragraph 91 The role of the Blood Transfusion Service in this respect was indirect. Every attempt was made to increase plasma procurement within the limits of funding provided by The Mersey Regional Health Authority (10). (See appendix A)

Paragraph 10e No research was carried out in The Mersey Regional Transfusion Service connecting Haemophilia with either Hepatitis or HIV.

Paragraph 10f & 11e The Consultant Haematologists and RTD's of Mersey and North Western Regions coordinated to form a Super Regional Haemophilia group, which met to discuss matters of policy relating to all aspects of Haemophilia care. The Mersey and North Wales Regional Transfusion Service expanded plasma procurement towards National self sufficiency in advance of completion of the new Blood Products Laboratory at Elstree in 1987.

- On the introduction of AIDS leaflets (which have subsequently been updated on a number of occasions) the Mersey and North Wales Regional Transfusion Service took steps to see that these were circulated to all donors from September 1983. They were available on sessions and circulated with donor invitations from that time.

- As soon as Factor VIII concentrate was prepared by the 8Y process it was heat treated and prepared from screened HIV negative plasmas. It was then made available to those responsible for Haemophilia Management for distribution.

- From October 14th 1985 all blood donations issued have been screened for HIV antibodies and found to be negative.

- From 1986 the information provided to donors about AIDS has included an enquiry about travel. Those who have visited West Africa have been screened for antibodies to HIV 2 - (the other virus which has been associated with AIDS) since April 1988.

Paragraph 91b Since the mid 1970's major consideration in planning for plasma procurement has been given to the provision of adequate supplies of Factor VIII concentrate for Haemophiliacs, but at the same time individual RTCS have had to balance this against the need for other products for local clinical use.

Paragraph 92a Regional Transfusion Directors met quarterly, since the earliest days of the NBTS, to coordinate planning of transfusion practices in England and Wales. From 1975 onwards plans were laid for self sufficiency in Blood Products derived from fresh frozen plasma (2,3,4,5,6,7), and in January 1977 a working group was appointed by the DHSS to establish future trends in plasma requirements (8,9,11). The Government then funded a new Blood Products Laboratory at Elstree with the capability to fractionate a volume of plasma which will make the Country self sufficient. Building work on the new factory commenced in 1983 and it was fully commissioned in 1987 (25), although various processes were operated in the interim.

- From 1983 when an association was made between Blood Transfusion and the Acquired Immunodeficiency Syndrome (AIDS) the National Blood Transfusion Service took pains to see that all measures to protect the National Blood Supply were taken in a co-ordinated manner and at the same time. e.g. a national leaflet was prepared for distribution on the same day (1st September 1983). Routine screening for HIV antibodies was introduced on one day (14th October 1985) and Consultants in the National Blood Transfusion Service were amongst the first to receive common instruction on AIDS counselling for the purpose of following up those donors found to be HIV positive.

- At the instigation of the NHS Management Board (18a), a survey was made of all the Regional Transfusion Centres in 1987 and a report submitted to the DHSS in 1988 (18b). The establishment of a National Blood Transfusion Service was one of three final recommendations made in this report. However proposals for a "National Director" came from within the NBTS in 1973 following reorganisation of the NHS that year (1). A need for better cordination of the NBTS was also recommended by the DHSS appointed working group at the end of their report of December 1977 (7).

- The disadvantage of a truly National Blood Transfusion Service is principally financial, since it was considered that such a move would require an increase in staffing and premises, with the headquarters probably in London. There was doubt as to the authority of a National Director and some individuals were not in favour of the uniformity and regimentation which might follow.

- The advantages are many:

  (i) A single policy would simplify techniques and donor practices.
  (ii) There might be considerable economies to be made in bulk purchases, e.g. blood packs.

(iii) Influence from the suppliers of source plasma would be greater upon the Blood Products Laboratory which fractionates that plasma.

- Documents available on this topic would include the report to the Department of Health and the policy statement of the National Director, Dr H H Gunson, who took up his duties on 1st October, 1988. Both of these will be available from Dr Gunson at The National Directorate in Gateway House, Piccadilly.

Paragraph 92 (b) Since 1975 needs for Factor VIII and IX have been determined on enquiry from the Director of The Haemophilia Service, who is based at the Royal Liverpool Hospital. Postholders to date since then have included Dr F E Boulton (1975 -1980), Dr B A McVerry (1980 - 1986) and Dr C Hay (1987 onwards). Such assessments are usually made at the time of planning for the annual budget. In the past these were revised according to deliveries received from the Blood Products Laboratory, there often being a need to embark on commercial purchases to make up the balance for therapeutic use. Details of blood products supplied, both NHS and commercial should be available in the Hospitals where patients were treated.

Paragraph 92 (c) Targets were set for the production of Factor VIII and Factor IX concentrate based on the current therapeutic practice and anticipated developments (e.g. elective orthopaedic procedures for deformed joints). Many years ago complicated orthopaedic procedures were only carried out in Oxford, which was the largest Haemophilia Reference Centre, and patients travelled to Oxford accompanied by their blood products.

- Targets were usually set by the Haemophilia Directors and plasma procurement tailored to provide them. These were monitored by all parties concerned, including the Haemophilia Society.

- The plans for plasma procurement will be minuted in the Meeting of the Regional Transfusion Directors (2,3,4,5,6,7,8,9,11,13). They also feature in some of the bids for monies of the Regional Transfusion Centres to their Health Authorities. In the Mersey Region this will probably be represented in the minutes of the RHA/RTC Working Party.

Paragraph 92 (d) The collection of blood is determined by red cell requirement and needs for plasma procurement. These are usually determined by Regional Transfusion Centres and recruiting drives undertaken to accommodate targets set.

- In The Mersey Region this information is documented in the short term plans and in the RTC/RHA Working Parties. In 1977 Dr Rosemary Biggs, an international authority, made an estimate for Haemophilia Treatment of 42 million i.u. of Factor VIII per annum (19). The amount of Factor VIII concentrate produced in 1978 will be recorded at the Blood Products Laboratory at Elstree, whose Director is Dr Richard Lane.

Paragraph 92 (e) Additional monies were received from time to time from 1975 to increase plasma procurement with a view to increasing Factor VIII production. The amount of money allocated is recorded in the short term plans for the Mersey and North Wales Regional Transfusion Service. Its funding included the provision of a special laboratory for processing blood at headquarters.

- The Mersey Regional Transfusion service did not have contact with the Scottish National Blood Transfusion Service who provide facilities for plasma fractionation, because the Plasma Fractionation Laboratory (PFL) in Scotland adopts a different working practice appropriate only for their own service.

Paragraph 92 (f) From time to time whole blood and plasma reduced blood has been obtained from the Scottish National Blood Transfusion Service (SNBTS) in common with other Regional Transfusion Centres in the United Kingdom. By contrast, however, clotting factor concentrate and plasma products have not been obtained from Scotland for use in this Region.

Paragraph 92 (g) & (h) The details of the size of donor pools in 1977,modifications of their size and consideration to such modifications determined at the Blood Products Laboratory at the start of plasma fractionation. The information therefore would be most accurately obtained from Dr Richard Lane in the Blood Products Laboratory at Elstree. These questions are ambiguous as they refer to donor pools (people) rather than donation pools (packs). From 1981 single donations of fresh frozen plasma were returned to Elstree in individual international plasma packs. The pooling of time expired plasma at the Regional Transfusion Centre before despatch to Elstree was gradually phased out in the Mersey Region. This measure together with RIA screening for Hepatitis B surface antigen was introduced to improve the quality of source plasma. Tests of increased senstivity for microbiological screening e.g. RIA (Radio Immunoassay) were needed to ensure minimal risks of transfusion transmitted disease. Both these measures were introduced to allow a more advanced process of Factor VIII production which required a large volume of raw plasma as starting material (9).

Paragraph 92 (i) At an educated guess less than 50% of Factor VIII produced was home produced in the late 1970's. From 1978 attempts were made to increase plasma procurement with a view to national self sufficiency. (See article by Dr H H Gunson in Health Trends - 17)

Paragraph 92 (j) The level of home produced Factor VIII fell between 1984 and 1985 while techniques for heat treatment to eradicate transfusion transmissible viruses were perfected. At the time it was felt inappropriate to issue non-heat treated NHS product made from plasma unscreened for HIV antibodies. Once the heat treated product was available from the Blood Products Laboratory no other sort of Factor VIII concentrate was issued by BPL for therapeutic use. Consideration was given to the use of heat treated Factor VIII and Factor IX certainly from 1982. At that time heat treatment was planned to eradicate non A non B Hepatitis.

- Pasteurisation which has been successfully applied to Human Albumin Solutions, is unsuitable for factor concentrates since it destroys their coagulation activity. An alternative technique was needed in order to eradicate resistant viruses which may be transmitted in blood. Early commercial products marketed to promote the benefits of their heat treatment have included some where the latter was inadequate and viruses have been transmitted in the products sold, e.g."FACTORATE" (16) . The 8Y process was designed by the Blood Products Laboratory at Elstree to exclude Non A Non B Hepatitis from their factor concentrates and a trial on "virgin" haemophiliac patients to date has shown 100% success. The treatment which is effective in dealing with the virus which causes Non A Non B Hepatitis also eradicates HIV.

- Human Albumin Solutions have been pasteurised for many years - certainly since the 1970's. Until recently they were issued as "Plasma Protein Fraction" but have recently been renamed Human Albumin Solutions.

- The techniques for heat treatment of plasma products are varied and correspondingly the benefits for their protection varies. As outlined above the 8Y process appears satisfactory to date in dealing with Hepatitis B, Non A Non B and HIV infections. The earliest work on heat treatment of Factor VIII concentrate was reported from Texas and presented at the combined meeting of the International Society of Blood Transfusion with the International Society of Haematology at their Congress in 1982 (20). The first reports of multi transfused patients acquiring Immunodeficiency were reported in the Lancet in 1983. At that time HIV had not been identified. It is possible that some suspicion about the Blood Products might have been roused in the United States in 1982 but we do not believe that this was prominent in The United Kingdom at that time.

- Factor VIII and Factor IX are both coagulation or "clotting" concentrates; there are many others.

- As far as we know heat treated concentrate was not available in West Germany from 1980 although it was available in America from 1982. Even though it was available there is no evidence to indicate just how effective it was in eliminating transfusion transmitted viruses. Such a process was under development in the United Kingdom but was not perfected until 1985.

Paragraph 92 (l) No work was undertaken into the development of heat treatment of Factor VIII and Factor IX in concentrates in the Mersey Regional Transfusion Centre. It would not have been appropriate on the small scale.

Paragraph 92 (m) Factor VIII and Factor IX concentrates of the heat treated variety were not used from 1980 for the reasons outlined above. The efficacy of the heat treatment was not proven and the material was imported, and none of them had a U.K. product license.

Paragraph 92 (q) It was appreciated from 1983 within the Blood Transfusion Service that some people are at higher risk from HIV than others as blood donors. The first Information Leaflet was prepared nationally for circulation in September, 1983, and has been updated several times since then (22 a - d).

- Categories of donors recognised in 1989 to be at higher risk are as follows:

  Homosexual/Bisexual males
  Intravenous Drug Users
  Prostitutes
  Travellers to Africa since 1977 who have had sexual relations with local inhabitants (heterosexual or homosexual)
  Sexual partners of Haemophiliacs
  Recipients of blood transfusions in Africa since 1977
  Sexual partners of the above categories

  As you will see high risk categories are not limited to homosexual/ bisexual males and drug addicts.

- Since September, 1983 leaflets have been circulated to all blood donors identifing all those at high risk. Everyone who has given blood since screening was introduced has signed a written disclaimer to indicate that they are not in a category of increased risk and that they understand and consent to their blood being tested for antibodies to the Human Immunodeficiency Virus and that if they are found to be positive they will be told so.

- In the Mersey Region Dr Shepherd prepared a notice for circulatio to clinicians for advising patients about the risk of transfusion transmitted disease (24). A leaflet prepared in the Welsh Region was also circulated for information to the Consultant Haematologists (23)

Paragraph 16 (61)

Information from the DHSS was conveyed to the Regional Transfusion Directors at their quarterly meeting as it became available by the Department Adviser Dr H Gunson (13). The Direction of the National Blood Transfusion Service was determined in discussion by that body and policy implemented as appropriate. Care was taken at all stages to see that the Regions present uniform approach and that developments were made in all Regions at the same time. For example: circulation of leaflets, HIV screening, AIDS counselling, follow-up of HIV positive transfusion recipients etc.

Paragraph 92 (r) Donations were not accepted from individuals who declared a history of a high risk group in Liverpool and North Wales. Although there was no policy of destroying or marking blood offered by donors revealing such a history, whenever a third party considered that such an individual belonged to a high risk group a destructive policy was adopted after examination of the facts.

Paragraph 93(s) The first DHSS leaflet of September 1983 about AIDS was received in the Mersey Region and distributed on Sessions. Various advisory documents have been circulated to Doctors by the Department of Health concerning AIDS since January 1985. Some of them however were completely unrelated to Blood Transfusion, e.g. HIV in breast milk. All such documents should be in the possession of Doctor Peter Simpson, the Regional Medical Officer. In general the advice received from the Chief Medical Officer from the DHSS followed a policy which had been conveyed to the Regional Transfusion Directors by the Departmental Adviser on Blood Transfusion rather than preceding it.

- Routine screening of all blood donations for antibodies to the Human Immunodeficiency Virus was implemented on Monday 14th October, 1985. The leaflets about AIDS were updated in September 1985 (22c) with details of testing, for issue to coincide with the introduction of HIV antibody screening.

Paragraph 74 Routine screening was introduced much earlier in the United States of America. It was not recommended here because appropriate confirmatory testing was not available for follow up of donors found to be HIV positive until the Autumn of 1985. We were strongly advised in this Country by our colleagues in America not to introduce a screening test in the absence of adequate confirmatory testing. This had led to serious clinical problems in the States in the intervening months.

Paragraph 92 (t) Routine testing for antibodies to HIV 1 was introduced as indicated above. All blood donations are tested everytime a donor comes. The new policy is documented both locally and in the minutes of the Regional Directors Meetings.

- Even now testing for HIV antigen is a highly specialised investigation available only through the Public Health Laboratory with appropriate clinical indications.

  Reliable tests for screening were not really available until 1985. Since the virus was only isolated in the Summer of 1984, it would be difficult to see how any specific tests could have been available at that time.

- In 1983 before the virus had been isolated, or even the nature of the disease as an infection proven, surrogate tests were identified which might indicate those who might run a similar risk (21). These included serological test for syphilis e.g. VDRL and antibodies to Hepatitis B core antigen (which is sometimes transmitted venereally). In this particular context surrogate tests bear little relation to the Human Immunodeficiency Virus and are merely performing a role similar to the AIDS leaflet in identifying people in a certain risk category rather than any proper evidence of the HIV infection concerned. Such surrogate tests are of a general nature and have been available throughout the 1980's, but kits for testing to antibodies to the Human Immunodeficiency Virus were available in the United States in March 1985.

Paragraph 92(u)

The Department of Health undertook a study of HIV antibody screening in Regional Transfusion Centres on a pilot basis in the Summer of 1985 before routine screening was introduced. This allowed for an evaluation of kits available and a report of this should be available from the DH or the National Directorate.

Paragraph 92 (w) The risks of Hepatitis to haemophiliacs from factor concentrate was appreciated by me (Dr V J Martlew) in 1981. I recognised a risk with raised serum alanine transferase in haemophilia reflecting a probable attack of acute non A non B Hepatitis which was usually sub clinical in the patients concerned after treatment.
Occasionally painless jaundice was seen as a proportion progressed to chronic liver disease. I believe that this was recognised much earlier by those more experienced in the field than I. (Dr A J N Shepherd was aware of this in 1976).

The risk of contracting Hepatitis from some types of Factor VIII concentrate was very considerable - probably in excess of 95% in the early 1980's. This risk was substantially greater for Haemophiliacs treated with imported commercial concentrates. These facts must have been clearly recognised by 1981 when plans were laid to develop the 8Y process for heat treating Factor VIII Concentrate at the Blood Products Laboratory to eliminate the risk of Non A Non B Hepatitis transmitted in Blood Products.

Paragraph 92 (y) I was aware of Acquisition of Immunodeficiency in November 1981 as a result of a referral for Bone Marrow examination by a exceedingly astute Physician who had read an early article in the New England Journal of Medicine. Since I was not employed in the Transfusion Service at the time my actions in the light of that knowledge are not relevant to this case. I must emphasise, however, that my awareness of AIDS in 1981 was not associated in my mind with the emergence of a new transfusion transmitted disease.

Paragraph 92 (z) Developments were reported rapidly in the American Literature to start with. The New England Journal of Medicine at that time was probably the best source of information for me.

From 1983 the British Literature kept apace of events, e.g. Lancet, BMJ.

Paragraph 92 (aa) The connection of AIDS and Blood Products became apparent in the United Kingdom in 1983 having been reported in the Lancet earlier in the year. In fact the association between AIDS and Blood Products was first reported in Haemophiliacs and followed up closely by those who had received cellular components. Following review of the original published data and subsequent developments there was little reason to doubt the link between blood and AIDS. No literature was published from the Mersey Regional Transfusion Service concerning the link.

Paragraph 92 (ad) Steps taken in the Mersey Regional Transfusion Service were in line with the National Policy determined by the Regional Transfusion Directors on advice from the Departmental Adviser Dr H Gunson. The articles in the Lancet of the 15th, 22nd, 29th January, 1983 have been reviewed. It is difficult to recall at this stage whether these particular articles were taken in by us at the time though they do not look unfamiliar now. The one of the 29th January does however "ring a bell". It certainly has been read subsequently. In the light of the information presented so far this claim is unreasonable.

Paragraph 92 (ac) Plasma procurement was expanded within the limits of financial constraints (Appendix A). Plasma was sent to the Blood Products Laboratory for fractionation to produce NHS Factor VIII concentrate. The more of the latter that was produced in the United Kingdom, the less the need to use imported non heat treated Factor VIII.

- Questions concerning advice about therapeutic alternatives in the use of factor concentrates are best directed to the Haemophilia Directors.

We hope these answers are of some help in your work. Copies have been submitted to the National Director and the Medical Defence Union.

Attached is a list (appendix B) of appropriate documents which are referred to in our response.

Dr V J Martlew

Dr A J N Shepherd

December 1989