Witness Name: Elisabeth Mary Buggins

Statement No.:WITN1021001

Exhibits: WITN1021002 - WITN1021013

Dated 18 November 2020

INFECTED BLOOD INQUIRY

EXHIBIT WITN1021004

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(2)

MEDICAL REPORT AND OPINION

Re: Jonathan BUGGINS GRO-C

DOB: GRO-C 80

GRO-C **WEST MIDLANDS.**

This medical report has been prepared from photocopies of the full case records of the patient obtained from The Children's Hospital, Ladywood Middleway, Birmingham.

The boy first presented at the hospital on 29.03.80 with symptoms of lower gastrointestinal bleeding. No obvious family history of a bleeding disorder was obtained although the boy's elder brother Richard had severe haemophilia complicated with a factor VIII inhibitor, and subsequently a younger brother with severe haemophilia. Clinical examination was unremarkable and coagulation investigations performed at the time demonstrated that Jonathan also had severe haemophilia (letter Dr. Hill to Dr. Sherlock dated 02.04.80). The boy was admitted for observation and no factor VIII preparation was given (summary letter Dr. Brown dated 25.04.80). The child experienced his first clinically significant haemorrhage on 13.02.81 with a bleed into the left ankle joint. He was treated at the hospital with 3 packs of cryoprecipitate with good effect. On 27.03.81, the boy sustained an injury to the left leg with bruising of the upper third, and from the treatment records it would seem that the child was given 234 units U.S. commercial factor VIII (Armour-batch U 95107). As cryoprecipitate treatment of infants was the recommended policy of the hospital and indeed nationally, the administration of this large donor pool commercial material in

preference of cryoprecipitate or NHS concentrate without authorisation was negligent. Review the following day (28.03.81) led to the administration of a further 234 units of Armour factor VIII (U 95107) but no clinical details are recorded. On 02.05.81, the child was then treated with 420 units Armour factor VIII (batch U 16109) for haemorrhagic symptoms in the right buttock. As before, there is no evidence that authorisation was given to depart from hospital policy, and it is remarkable that a different batch of U.S. material was given. On 12.05.81, a mouth bleed was treated with 5 packs of cryoprecipitate and the child was admitted for observation. On 24.05.81, a similar bleed in the mouth was managed with 218 units Armour factor VIII (batch U 99108); on 14.08.81 a bleed into the left buttock led to treatment with a further batch of Armour material 210 units (batch U 15409), given as an O.P. with the comment that the boy was going to Shrewsbury on holiday the same day. On 06.09.81, the child was admitted with a head injury and treated with 3 packs of cryoprecipitate. Thus, during 1981, the child was treated on 9 occasions with, in total, 11 packs of cryoprecipitate and 1316 units large donor pool U.S. concentrate comprised of 4 totally different batches. During 1982, the boy was treated on 18 occasions with a total of 24 packs of cryoprecipitate and 4195 units Armour factor VIII comprised of 3 different batches. It is of note that on 20.05.82, it is recorded that no 0+ve cryoprecipitate was available, leading to the use of U.S. commercial factor VIII administration, yet on 13.07.82 a mixture of 0+ve and 0-ve cryoprecipitate was given, without adverse event. On many of the occasions when cryoprecipitate was given, the patient was not admitted to a ward indicating that convenience of administration of factor VIII concentrates over cryoprecipitate possibly obviating IP admission was not a cogent argument for their usage. During 1983, the boy was treated on 26 occasions, exclusively with Armour factor VIII (10,114 units) both as an IP and OP. During this year, 9 different batches of the Armour product were used. During 1984, the boy was

treated on 17 occasions, initially until 19.05.84 with 3190 units Armour factor VIII (4 different batches) then exclusively with NHS factor VIII concentrate - 3385 units. This change in policy was due to an allergic reaction to Armour product on 18.05.84. In 1985, only NHS material was used. In terms of HTLV III transmission, a retrospective test on stored samples demonstrated a positive antibody test in April 1983, subsequently confirmed by positive antibody results from samples tested in 1985 and thereafter. No negative testing samples were available in this case.

OPINION

This case concerns a young child with severe haemophilia who was treated with either cryoprecipitate or U.S. large donor pool commercial factor VIII concentrates between 13.02.81 and 19.05.84. Subsequently, the boy was treated exclusively with NHS factor VIII concentrates. Despite the fact that the first HTLV III antibody positive test result was obtained in 1985, retrospective antibody testing of stored serum samples demonstrated HTLV III antibody positivity on a sample taken in April 1983. No antibody negative samples were available, and it must be concluded that HTLV III transmission occurred between 1981 and early 1983.

There are several issues in this case which are divergent with established clinical practice:-

1. **Use of large donor pool U.S. commercial concentrates**

In 1981, when the patient experienced his first clinically significant bleeding symptoms requiring factor VIII replacement therapy, cryoprecipitate was given with a satisfactory therapeutic response and no adverse events. At this time, cryoprecipitate was the recommended form of factor VIII replacement therapy for the management of previously untreated infants with severe haemophilia and for

their subsequent management. Cryoprecipitate was of particular benefit in such cases since it was derived from single voluntary donor plasma collections in the U.K. and thus carried a substantially lower hepatitis B and non-A, non-B hepatitis risk, and was highly cost-effective for the 'on demand' management of small children in hospital. Furthermore, sufficient amounts of factor VIII necessary to control haemorrhagic symptoms in such small children were available in only a few single donor bags of cryoprecipitate. The somewhat larger infusion volumes with such treatments compared with the smaller reconstitution volumes of concentrates, were not considered to disadvantage the increased safety aspects of this therapeutic approach. Factor VIII concentrates, on the other hand, and particularly U.S. commercial material from paid donors, were derived from large donor pools (Elstree 3,500 donors, Oxford 500 donors, U.S. concentrate >10,000 donors - minutes p5. U.K. Haemophilia Reference Centre Directors Meeting, September 1980), and imparted a substantially higher risk of hepatitis. Furthermore, the increased morbidity in small children following infection with hepatitis B and non-A, non-B hepatitis was an additional reason for choosing cryoprecipitate over concentrate. Such large pool concentrates, especially the NHS material obtained from plasma pools from voluntary donors, were used in children when cryoprecipitate was not available, when the patient experienced allergic reactions to cryoprecipitate uncontrolled by antihistamines, or when a patient with frequent haemorrhagic symptoms became established on a home treatment infusion programme. This policy was seemingly that practiced by the Children's Hospital in Birmingham which was one of the largest Paediatric Haemophilia centres in the U.K., and such a policy document was distributed to all junior medical staff in the Haematology Dept. who could be involved in the treatment of patients with severe haemophilia.

On the second occasion that the child needed factor VIII replacement (27.03.81), the national recommendations and the hospital policy for haemophilia treatment were ignored, and U.S. commercial factor VIII concentrate was given. The clinical details of the boy's presenting symptoms and signs were minimally documented, but were obviously mild in nature and not of potential life-threatening proportions. No explanation whatsoever was given as to why cryoprecipitate or even NHS factor VIII concentrate were not used or even if they were not available in the hospital at the time. Furthermore, there is no documentation as to whether advice in the choice of therapeutic product was sought from a senior colleague, or whether authorisation was requested or given to administer this U.S. material. Treatment of the child with U.S. product, in view of the prevailing recommendations and hospital policy, the lack of suitable documentation and in the absence of authorisation was negligent. As the child had responded in an entirely satisfactory manner to the administration of only 3 bags of cryoprecipitate for an established left ankle haemarthrosis on 13.02.81, any argument that commercial factor VIII was given instead of cryoprecipitate to ensure a more predictable response is untenable. This is supported by the observation that cryoprecipitate was used quite often on subsequent occasions to treat more serious bleeding symptoms (e.g. head injury on 06.09.81) when haemostatic control based upon a predictable therapeutic response was vital. On 28.03.81, the child was seen again, and despite the record that the clinical condition 'seems to be settling down' a further 234 units of the same batch of Armour factor VIII was given, thus increasing the bioload of any potentially infectious agent in this material for treatment on minimal clinical indications. On 02.05.81, a similar situation arose where the boy was treated with 420 units Armour factor VIII for a bleed in the right buttock. No documentation relating to lack of availability of cryoprecipitate or NHS concentrate is available as also no record of authorisation. A different batch of Armour material was used on this

occasion exposing the patient to potentially infective agents derived from a further large range of U.S. paid blood donors who were untraceable. In contrast, some 5 weeks later, the child was treated with cryoprecipitate for a bleed in the mouth, which potentially is far more serious than those bleeds previously treated with concentrates, and correspondingly the boy was admitted for observation. Only 12 days later, a similar bleed was treated with commercial concentrate from a third batch while 3 months later a fourth batch was used. This haphazard and dangerous treatment pattern where therapy alternated between cryoprecipitate and U.S. commercial concentrate of various batches continued through until 1983. With the exception of one treatment occasion where it was documented that no cryoprecipitate was available (on 20.05.82), Armour concentrate was given without any record of authorisation, and no mention made of treatment policies or availability of NHS concentrate. Although 0+ve cryoprecipitate was most optimal for treatment in this case, a relatively low availability of this form of cryoprecipitate did not provide a sole indication for U.S. concentrate use, since on 13.07.82 a mixture of 0+ve and 0-ve cryoprecipitate was administered to the child with good effect and without adverse event. During 1983 and into early 1984, Armour concentrate was used exclusively although there is no satisfactory documentation to indicate that the boy had developed allergic reactions to cryoprecipitate uncontrolled by antihistamines, had shown any signs suggestive of reduced efficacy of cryoprecipitate or was established on a home treatment programme. This policy was pursued, with no reference to the availability of NHS concentrate at the hospital in the face of growing concern and increasing information in the public and medical press that AIDS was transmitted by blood products.

2. Specific comments on the therapy given prior to the retrospective seroconversion date.

As previously stated, the administration of large donor pool U.S. concentrate to such a small child without substantial clinical indication contravened the recommendations at both national and local levels. This practice was negligent and below the standard expected of a reasonably competent paediatric haematologist treating haemophilia patients. The belief that once the child had received one batch of U.S. concentrate, the risks could be minimised by continuing that batch, was fallaceous, as it became clear during the early 1980s that the bioload (the total amount of a batch given to any one individual) was a critical factor in terms of potential infectivity of a transmissible agent. Although it would seem that Dr. Hill, as a number of haemophilia treaters in the U.K. at this time, believed that continued use of the same batch confined the risk of infectivity, this was clearly not practised in the case of this child. This is evident from the fact that between 1981-mid 1984, 20 different batches of Armour factor VIII were used, and during the relevant period (1981-1982) when infection with HTLV III most probably occurred, some 7 different batches comprising the total unitage of 5516 units of Armour factor VIII were administered. This very small unitage, however, carried a very high potential for possible infection as the material from all these batches was probably derived from at least 70,000 paid U.S. blood donors. From this aspect, cryoprecipitate and to some extent NHS concentrate if used consistently would have imparted a far lower infectious risk, particularly as the Armour material originated in the U.S. where paid blood donations were the commercial companies plasma source, and where AIDS was believed to have originated and had already started to become manifest as a clinical entity in U.S. haemophilia patients.

It would seem that Armour was the sole supplier of commercial factor VIII to Birmingham Children's Hospital at that time, and Dr. Hill was purchasing large amounts (0.25-0.5 million units) of low unitage (200 units) vials at any one time. However, instead of allocating an individual small group of patients on any one batch to ensure long-term continuity of management of such cases on the same batch, it would seem that, with a few exceptions, the vast majority of Dr. Hill's patients received the same batch over a few months until the batch was used up. This rather bizarre approach to patient management resulted in the child receiving a relatively large number of batches of vials of material containing few units in a remarkably short time.

The therapeutic management of this child during 1981-1984, but particularly during 1981 and 1982 was negligent, and undoubtedly the ill-conceived use of Armour factor VIII must be held responsible for the infection of the child with the AIDS virus.

GRO-C

G.F. SAVIDGE, M.D.

Director, Haemophilia Reference Centre

2nd June, 1992.