Witness Name: GRO-B
Statement No.: WITN2151002
Exhibits: WITN2151003-020
Dated: 21st July 2021

INFECTED BLOOD INQUIRY

EXHIBIT WITN2151004

95 09:40 GRO-C PROF F E PRESTON

MEDICAL REPORT PREPARED BY

PROFESSOR F ER.C PRESTON, MD FRCP FRCPath

Prepared at the request of:

Paull & Williamsons. Solicitors

Re GRO-B

GRO-B

26 May, 1995

95 09:41 GRO-C PROF F E PRESTON

REPORT ON GRO-B dob GRO-B 31)
GRO-B

I have prepared this report upon the medical records provided to me from the Royal Infirmary, Edinburgh and the GRO-B, Edinburgh and at the request of Solicitors, Paull & Williamsons. I have been asked to comment particularly on the diagnosis of Hepatitis C in the above named boy, diagnosed with von Willebrand's disease.

S first presented with the clinical features of a bleeding disorder at the age of 19 months, when according to a letter written by a Dr GRO-B GRO-B and dated 15.7.83, he was admitted on account of a bleeding frenulum. The original injury had occurred two weeks earlier. According to his mother, he had tended to bruise easily since birth. There was no family history of a bleeding disorder. Simple screen tests of coagulation, presumably performed at GRO-B indicated a normal one-stage PTT and a PTTK of 59 seconds (control 38 seconds). Normal ranges for these tests are not quoted, but it is my view that the PTTK is significantly prolonged. There is no comment in this letter as to the likely diagnosis.

An entry in the GRO-B Edinburgh's notes, dated 15 July 1983 indicates that GRO-B was transferred from GRO-B with a "? bleeding disorder". The notes indicate that the diagnosis was " probable mild haemophilia". Tests of coagulation, presumably performed at the GRO-B GRO-B Edinburgh, indicated that the factor VIII level was 7½%. He was transfused with 180mls of blood on the 16.7.83 and discharged home on the 17.7.83 with a follow-up appointment to see Dr Ludlam in August 1983. An entry in the medical notes dated 20.7.83 indicates that he was given 250 units of factor VIII.

An entry in the medical records of the GRO-B Edinburgh, dated 20.7.83 indicates that he was admitted 2.35 am on that date. The diagnosis on admission was considered to be haemophilia. The entry also states that S was "transfused on Saturday". This presumably means a blood transfusion. The same entry also indicates that GRO-B was "Given 250u. Factor VIII". In my view, this means clotting factor VIII concentrate. In a later entry dated 7.30am on 20.7.83, there is a comment that he was "Still oozing + +". This indicates that the bleeding did not respond to the administration of the clotting factor VIII concentrate. For this reason, another dose of 250 units of factor VIII concentrate was asked for. On the following day, the 21.7.83, he received alternative treatment in the form of DDAVP, Tranexamic acid and cryoprecipitate. DDAVP is a synthetic vasopressin analogue, which is used for the treatment of patients with von Willebrand's disease, and also mild haemophilia A. The entry in the notes on the 21.7.83 indicates that the bleeding stopped following the administration of DDAVP and cryoprecipitate. The entry dated 21.7.83 also states "Factor VIII Rags ↓". I believe that this means that the factor VIII-related antigen level was reduced. The same entry also states "∴ Diagnosis is now Von Willebrand's disorder".

A Discharge summary dated 22 July 1983 signed by Dr GRO-B, Registrar indicates that S had bled excessively following a fall which resulted in facial injuries. Investigations revealed a factor VIIIC of 7½% and a haemoglobin of 7.3 g/dl. He received 180mls of blood and was discharged home on 17 July 1983. He was readmitted at 2.30am on 20 July, on account of bleeding from his lip following a further fall. On arrival he was given 250 units of factor VIII. The next morning his mouth was still oozing, and he was therefore given DDAVP and tranexamic acid. The discharge summary indicates that when the results of some additional blood tests came back from the Royal Infirmary, these indicated that the correct diagnosis was von Willebrand's disease.

On 3.10.84 S was admitted into the GRO-B Edinburgh, on account of having banged his head 24 hours previously. The clinical signs and symptoms suggested the possibility of an intra-cranial haemorrhage. Since it was known that he had von Willebrand's disease, he received intensive treatment with cryoprecipitate. A brain scan showed an area of increased density on the right side, which was thought to be due to a haemorrhage. He received cryoprecipitate until 18.10.84. According to the discharge summary, his total infusion of cryoprecipate from 3.10.84-18.10.84 was 34 units of cryoprecipitate. Blood levels of clotting factor VIIIC, von Willebrand and RAg and ristocetin cofactor were monitored following the administration of the cryoprecipate. Throughout the admission, the case records are extremely detailed and provide a comprehensive account of his clinical progression and also his management.

According to the discharge summary which was written by Dr O B Eden, Consultant Haematologist, S made very rapid improvement and "...by 7.10.84, he was neurologically normal.....". He was discharged home on 18.10.84. S was again admitted on 2.11.84 on account of having banged his head on a radiator after he had tripped whilst playing. He received 2 units of cryoprecipitate.

It is clear from correspondence from Dr C A Ludlam, Consultant Haematologist to Dr GRO-B GRO-B that S had recovered completely. I assume that Dr GRO-B General Practitioner.

In a letter dated 2.9.83 written by Dr C A Ludlam, Consultant Haematologist to Dr GRO-B GRO-B General Practitioner, Dr Ludlam states "We confirm that this boy has von Willebrand's syndrome, with a factor VIIIC of 0.06 units/ml, VIIIRAG less than 0.10 u/ml and ristocetin cofactor 0.43 u/ml." Dr Ludlam also indicated that he had issued S with

a DHSS Haemorrhagic States Card, stating that he has von Willebrand's disease.

It is clear from the correspondence in the notes that S attended the Haemophilia Unit at the Royal Infirmary, Edinburgh on account of a number of nosebleeds. This is not an uncommon manifestation of von Willebrand's disease. He received treatment with DDAVP and Cyclokapron. A letter dated 6.3.84 written by Dr Mary Judge, Registrar in the Haemophilia Unit, Royal Infirmary of Edinburgh to Dr GRO-B indicates that the bleeding did not respond to DDAVP and he was therefore given intravenous cryoprecipitate which effectively controlled the bleeding and kept under observation. He was discharged from hospital the following day.

The medical records indicate that S received Haemate P in August 1993 to cover a dental extraction in order to relieve dental crowding. Haemate P is a clotting factor concentrate which is of known value for individuals with von Willebrand's disease. On the 24 August 1993, he attended on account of bleeding from his gums, which was associated with a loose tooth. A dental extraction was performed after the administration of DDAVP, but this failed to control the bleeding.

In January 1995, he also received Haemate P to cover a dental extraction.

A letter to Dr GRO-B written by Dr Rosemary Dennis, Clinical Assistant to Dr C A Ludlam, dated 27.8.93 indicates that Mrs GRO-B was concerned about the viral safety of blood products, and she asked whether it would be better for S to be given cryoprecipitate. Following discussion and with her consent S was given was 1,000 units of Haemate P.

HEPATITIS C

A [illegible] entry in the clinical notes dated 31.5.93 states "Hep C +ve to be discussed [illegible]eeds liver bloods". A later entry dated 29.12.93 states "I didn't discuss with [illegible] ; am unable to read this word) Hep C status". An entry in the clinical notes dated 3.2.94 reads "Send appt (appointment) for Liver Clinic 1.3.94 9.30 am HCV PCR +ve.

There is a letter dated 3.2.94, written by Dr C A Ludlam, Consultant Haematologist, to Mr & Mrs GRO-B informing them that he holds joint clinics with Dr Peter Hayes, a liver specialist at the Haemophilia and Haemostasis Centre, and inviting them to bring S to this liver clinic on 1 March 1994. It is clear from the medical records that S attended this clinic, together with his father on 1.3.94. An entry in the clinical notes for the outpatient visit reads "Father present. Full information about Hep C infection, natural history of the disease, investigations and treatment with Interferon." On 1.3.94, Dr Peter Hayes, Senior Lecturer to Dr Christopher Ludlam, indicated that he (Dr Hayes) had seen S together with his father at the Haemophilia/Liver clinic. The letter further indicates that he explained to GRO-B that S "....had hepatitis C and abnormal liver function tests". The letter also indicates that discussions took place about the virus (hepatitis C virus) and that S was given some literature to take away.

In the clinical notes, there is also a check-list for Interferon therapy dated 1.3.94 in which it states :-

1. Discussion of hepatitis C and Interferon.
2. Seen at liver clinic.
3. Hepatitis C information sheet given?
4. Screening blood tests for other causes of liver disease taken?

On the same date there are three items ticked -

14. Interferon treatment scheduled explained?

15. Expected response rate to Interferon discussed?

16. Side effects of Interferon discussed?

An entry in the notes dated 29.3.94 indicates that Mr and Mrs GRO-B were both present at the Liver Clinic, and that there was a further full discussion about hepatitis C. The entry also reads "To commence interferon next week". The clinical notes indicated that the Interferon to be used was Roferon-A.

A letter dated 29.3 94 from Dr Janet Andrews, Clinical Assistant to Dr C A Ludlam and addressed to Dr GRO-B General Practitioner, indicates that discussions had taken place on that date, the 29 March 1994, with Mr & Mrs GRO-B The letter further indicates that the parents had agreed for S be treated with Interferon, three times weekly, for an initial period of six months. Arrangements were made for S and his parents to attend on 5 April 1994, for instruction in the administration of this drug.

On the 27 September 1994, Dr Janet Andrews wrote t GRO-B informing him/her that S had been on Interferon for five and half months and that throughout this period his ALT values (liver enzymes) had remained slightly elevated throughout. She also stated that there had been no change in quantitative hepatitis C PCR during the six months treatment. This is a test which quantifies the amount of virus present in the blood. As a consequence of this observation, Dr Andrews had informed Mrs GRO-B that S had not responded to Interferon and the treatment was therefore discontinued.

An entry in the clinical notes dated 27.9.94 reads "Quant. PCR. No response. Mother told

this, ∴ TO STOP."

A NUMBER OF LETTERS HAVE NOT COPIED WELL THESE INCLUDE:-

One to Dr GRO -B from Dr Ludlam dated 8 September.

One to Dr Thores dated 8 September 1983

One to Professor Sutcliffe dated 12 September 1983

There are a number of reports from the Department of Clinical Chemistry at the Royal Infirmary, Edinburgh during the period 10.8.83 - 6.1.95. These provide detailed information relating to liver function tests. The second report dated 15.5.85 indicates a Alanine aminotransferase (ALT) level of 54 u/l. Normal range is quoted at 10-40 units/l. This is a slightly abnormal result. A report dated 2.6.94 from the Department of Clinical Biochemistry, Royal Infirmary, Edinburgh provides cumulative data and indicates that S had intermittently elevated liver enzyme levels during the period August 1993-June 1994.

Reports from the Department of Clinical Biochemistry at the Royal Infirmary of Edinburgh indicate that during the period August 1993-January 1995, liver enzymes were performed on approximately fourteen (14) occasions and on eleven (11) of these, the enzyme level was slightly increased.

COMMENT

It is clear from the medical records that S is HCV-antibody positive. There is an entry in the notes which indicates this and is dated 31.5.93. The fluctuating abnormal liver enzyme results are consistent with a diagnosis of chronic HCV-related hepatitis.

It is extremely likely that S acquired the virus through the administration of

blood products. Possible candidates are 1) a blood transfusion, 2) cryoprecipitate, 3) clotting factor concentrates. In view of the very large number of donor units which are included in the manufacture of clotting factor concentrates, the last named is the most likely source of the infection. A single blood transfusion is the least likely.

The most likely source of HCV infection was the concentrate that was used in 1983, (during his first admission). In 1993 S received another clotting factor concentrate, namely Haemate P. This is a virally inactivated product and it is very highly unlikely that this transmitted hepatitis C virus. Moreover, it was administered after the HCV-antibody positive status had been established in GRO-B

Regarding the use of cryoprecipitate, it is my view that at all times this was entirely appropriate, both in respect of frequency and intensity of treatment.

Until three or four years ago, the treatment of choice for individuals with von Willebrand's disease was 1) DDAVP and 2) cryoprecipitate. DDAVP is a synthetic therapeutic agent which is not derived from blood products. A substantial proportion of individuals with von Willebrand's disease respond satisfactorily to this agent. For those patients who fail to respond, or only partially respond, cryoprecipitate was, until recently, the treatment of choice. Approximately, three or four years ago, the UK Haemophilia Centre Directors Organisation recommended against the use of cryoprecipitate on the grounds that it is not virally inactivated and therefore has the potential of transmitting viruses, particularly hepatitis C virus. Currently, therefore, where DDAVP is ineffective, virally inactivated clotting factor concentrates are the treatment of choice. For individuals with von Willebrand's disease, these need to be carefully selected. The virally inactivated product Haemate P is a recognised product for the treatment of patients with von Willebrand's

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disease.

[redacted] 1983 S was treated with clotting factor concentrate in the Royal [redacted] for Sick Children, Edinburgh, on the assumption that he was suffering from mild haemophilia. This was based on a low level of factor VIIIC. The distinction between mild haemophilia and von Willebrand's disease is made on the basis of family history, and additional blood tests, notably, the measurement of von Willebrand factor. At that time, in 1983 when he first presented, the appropriate assays were von Willebrand factor antigen assay, and ristocetin cofactor assay. When Mr S first presented at 4.00 am on that date, the von Willebrand assays had not been performed and at that time, the diagnosis was considered to be mild haemophilia. He was therefore treated with a clotting factor concentrate which failed to control the bleeding. It was only some time later that the results of the von Willebrand factor assays became available, and the diagnosis of von Willebrand's disease was established.

Although the initial treatment with clotting factor concentrate was based on a false premise of a diagnosis of haemophilia A, it should be appreciated that in the early hours of the morning, laboratory tests to distinguish between haemophilia A and von Willebrand's disease are unavailable. Also there was no established diagnosis within the family and it wa[redacted] S irst clinical presentation. If the severity of the bleeding at that time of the day was sufficient to warrant immediate treatment, then the administration of factor VIII concentrate to an individual known to have a factor VIII level of 7½% whilst inappropriate, is nevertheless, understandable.

GRO-B

26 May 1995