

Witness Name: Debra Pollard

Statement No.: WITN3094052

Exhibits: WITN3094054-055; WITN3094127-128

Dated: 2023-08-18

INFECTED BLOOD INQUIRY

EXHIBIT WITN3094055



Pond Street
Hampstead
London NW3 2QG

The Royal Free Hospital

GRO-B

The Katharine Dormandy Haemophilia Centre & Haemostasis Unit

Directors:

GRO-B

Dr E.G.D. Tuddenham, MRCP, MRCPath.

Ref: PBAK/cb

16th May 1984

GRO-B

Dear GRO-B

Re: Miss GRO-B d.o.b. GRO-B Hospital No: GRO-B
GRO-B
Mr GRO-A d.o.b. GRO-A Hospital No: GRO-A
GRO-A

I apologise for the delay in writing to you about our further investigations on GRO-B and GRO-A whom I saw on GRO-B

GRO-B seems to have generally improved over the last three months. Her surgical neck wound has now healed, and she feels generally well. She did mention that she had had a few mild episodes of left sided nose bleeding which had responded to local measures. Also, her acne had been rather worse than usual. She had also noticed two 1cm diameter soft, painless subcutaneous nodules on the back of her neck which she thought were resolving spontaneously.

A repeat set of tests gave the following results:

		Normal Range
PT secs	13	(11-14)
PTTK secs	46	(30-40)
Patient/control mix	38 (c=34)	
Fibrinogen (clot wt) g/l	2.1	
Thrombin time secs	18	(14-16)
Reptilase time secs	16	
VIII:C u/dl	40	
VIII:R Ag u/dl	105	
VIII:RiCoF u/dl	107	
IX u/dl	50	
Inhibitor screen (1 hr PTTK)	Negative	
VIII multimer sizing	Normal	
V u/dl	120	
VII u/dl	140	
X u/dl	94	

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An International Training Centre of the World Federation of Haemophilia

Re: GRO-B
GRO-A

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Template bleeding time mins	14½, 18
Platelet count 10 ⁹ /l	153
Platelet aggregation %	
ADP 2 µM	25
ADP 3 µM	35
ADP 10 µM	55
adrenaline 2 µM	55
collagen 1 µg/ml	8
collagen 2 µg/ml	38
ristocetin 1.25 mg/ml	90
ristocetin 0.5 mg/ml	8

As you will see, there were some differences compared with our previous findings. The basal factor VIII:C level was higher at 40 u/dl; and the factor V and factor X levels are now clearly normal. The factor IX level, although still borderline, is also higher than we measured previously. The bleeding time was still prolonged; in-vitro platelet aggregation was not as brisk as previously (when Miss GRO-B was receiving cryoprecipitate therapy), showing some impairment of second phase aggregation. Unfortunately, we were unable to measure platelet adenine nucleotides because of machine failure. A factor VIII multimer sizing analysis showed a normal pattern.

Because I thought it might be useful for future management, GRO-B was given a test dose of 20 µg DDAVP (desmopressin). The time course showed:

	VIII:C (u/dl)	Bleeding time (mins)
Pre:	40	14½, 18
30 min post:	90	13
2 hr post:	80	19
4 hr post:	76	-
22 hr post:	34	-

As you see, VIII:C values rose to 2-3 times baseline within two hours, but had fallen to baseline at twenty two hours. The bleeding time seemed unchanged.

In addition to carrying out these tests of haemostasis, I also arranged routine blood count and biochemistry profiles (copies of report sheets attached). The blood count was normal, but the biochemistry screen showed changes typical of acute post-transfusion hepatitis - you will note that enzyme results were considerably elevated above normal ranges. In view of the fact that previous serology has been negative for hepatitis B, I think it most likely that GRO-B has contracted acute non-A, non-B hepatitis as a result of the intensive therapy she was given with factor VIII concentrate,

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plasma and cryoprecipitate.

I think it very likely that the higher baseline level of VIII:C which we measured (40 u/dl compared with 9 u/dl) is consequent on this acute hepatitis, and in all probability this accounts also for the higher level of VIII:RAG. An additional complication is that the acquired coagulopathy, possibly consequent on propylthiouracil, may not have yet entirely resolved, although the increased levels of previously depressed clotting factors suggest that there has been a general improvement in this respect.

Because of these complicating factors, a definitive conclusion about GRO-B's baseline bleeding state is not easy to make. However, the higher levels of VIII:RAG and VIII:RiCoF than VIII:C, the rapid rate of fall-off in VIII:C after cryoprecipitate and DDAVP, the normal multimer sizing pattern, and the family history are findings which strongly suggest that GRO-B is a carrier of haemophilia A. While the long bleeding time would be more in accord with von Willebrand's disease, there is very little else to suggest this diagnosis. It could be that the mild platelet function abnormality contributes to this long bleeding time; also, it might still partly represent some effects of propylthiouracil. Additionally, I should mention that we have several women under our care who from all points of view must be carriers of haemophilia, but who have long bleeding times. I do not have a pathogenetic explanation for such defects.

Working on the assumption that Miss GRO-B is a carrier of haemophilia A, I talked to her and her fiancé in some detail about the implications of this. I emphasised that although she would have a one in four chance of having a haemophilic son, the severity of such haemophilia was likely to be similar to that of her brother - in other words, clinically rather mild.

So far as management of her hepatitis is concerned, I would suggest that all that is necessary is to check her liver function tests occasionally. We have found that although patients may remain asymptomatic, test abnormalities may persist for many months. Hopefully, the abnormalities will gradually resolve if further blood product therapy can be avoided. If, because of a bleeding problem, therapeutic intervention should be thought to be necessary, I think it would be well worthwhile considering a trial of DDAVP. GRO-B has been given a small supply of this agent to take back to Turkey and if there are problems in obtaining more I should be happy to try and help.

The position with GRO-A is much more straightforward. As you know, he has a clinical history suggestive of moderately severe haemophilia, in that bleeding has largely been confined to surgery and trauma. I note, however, that he had a circumcision as a child without trouble.

GRO-A's joint problems are in his right ankle and right elbow. In August 1983, he suddenly developed severe pain and limitation of movement in his

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ankle. There was no particular history of injury, but he is an active sportsman and had been wind-surfing in the preceding period. Since that time, he has had intermittent aching pain in this joint which has caused him some problems with walking, and limited his ability to play sports. The right elbow problem is more longstanding. Some ten years ago, he injured this joint while exercising with springs. He gets occasional arthritic pains, especially in cold wet weather and has a mild reduction of flexion/extension.

The results of our tests showed:

Blood group	O Positive
PT secs	12
PTTK secs	61
Patient/control mix	40 (c=34)
Fibrinogen (clot wt) g/l	2.3
Thrombin time secs	16
Reptilase time secs	14
VIII:C u/dl	4
VIII:R:Ag u/dl	70
VIII:RiCoF u/dl	76
Inhibitor screen (1hr PTTK)	Negative
Multimer sizing	Normal
Template bleeding time mins	6', 6'
Platelet count 10 ⁹ /l	147
Platelet aggregation %	
ADP 2 μ M	63
adrenaline 2 μ M	60
collagen 1 μ g/ml	75
ristocetin 1.25 mg/ml	88
ristocetin 0.5 mg/ml	5

These results are typical of moderately severe haemophilia A. Mr GRO-A was somewhat surprised that we had found his factor VIII:C to be as low as 4 u/dl, in view of the fact he has had so little bleeding. I think his good general health, consequent on a high level of fitness due to his sporting activities, has contributed to his lack of serious problems.

While he was here, Mr GRO-A had a consultation with my colleague Mr J Colin Madgwick, Senior Consultant Orthopaedic Surgeon. Mr Madgwick felt that it was impossible to say whether Mr GRO-A's joint problems were consequent on bleeding, although this seems a possibility. He noted a small right ankle effusion, pes planus, and limited flexion/extension at the right elbow. There were minimal changes on the ankle x-ray. A number of measures were suggested, including weight reduction, wearing arch supports for the feet, and the selection of suitable sporting activities - running and football seem inappropriate. A programme of

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physiotherapy might also help, and Mr GRO-A has been instructed about suitable exercises by our physiotherapist.

As regards the management of bleeding problems, it seems clear that surgical procedures and bleeding which may follow trauma will have to be treated, as previously, with factor VIII concentrate. I did discuss the problems of concentrate with Mr GRO-A particularly those like hepatitis which are likely to be at least partly consequent on the large donor pools from which the concentrate is prepared. If at all possible, and if only a limited amount of therapy is needed, I suggested that Mr GRO-A might look into the possibility of obtaining cryoprecipitate. I do not know whether this product is obtainable in Istanbul, but I understand that at least one of the commercial companies might produce freeze dried cryoprecipitate made from relatively small donor pools. If it is possible to obtain such material, I think it might carry less risks. The problem with hepatitis may be resolved in the near future, since great efforts are now being made to develop procedures for sterilization. Heat-treated concentrates are currently undergoing clinical trial and the preliminary results are encouraging.

Mr GRO-A has a two year old daughter, GRO-A who I understand was recently tested in the USA. She will of course necessarily be a carrier of haemophilia and in view of her aunt's low factor VIII level, it will obviously be of relevance to know whether GRO-A is similarly affected.

While I don't think there is any necessity for me to see GRO-B again, I should be interested to repeat some of our tests in about a years time if she is ever passing through London, and I should of course be pleased to try and help if there are any problems.

With all best wishes

Yours sincerely

GRO-B MD, MRCP
Consultant Haematologist

Encs.