EDGWARE GENERAL HOSPITAL
EDGWARE, MIDDLESEX
HA8 0AD 01-952 2381

Hendon Group Hospital Management Committee

Apt 5pm
19th Feb
9.30 a.m.

SA/BMT 29th January, 1974.

GRO-C: KRD

Dr. K. Dormandy,
Department of Haematology,
Royal Free Hospital,
Lawn Road,
London, N.W.3.

Dear Kate,

Re: GRO-B (D.O.B. GRO-B 59)
GRO-B

This boy presented here for circumcision in August 1968, but was known to be a haemophiliac, first diagnosed in 1960 at the West Herts. Hospital, and subsequently confirmed at U.C.H. We found that he was mildly affected (AHG level of 8%) and his operation was uneventful with cryoprecipitate cover. He has subsequently had other minor episodes of bleeding and dental extractions, well controlled by us. We have never found an inhibitor. There is a strong family history of haemophilia.

He is now too old for paediatric care, and I thought it would be wise for him to come under the care of an official Haemophilia Centre. I would, therefore, be very grateful if you could see him with this in mind; his next of kin is Mrs. GRO-B Of course, we will continue to cope with the minor episodes at this end if you so desire.

Kind regards,

Yours sincerely,

GRO-C

S. Ardeman
Consultant Haematologist

THE HAEMOPHILIA CENTRE,

187,

Ext. GRO-C

KMD/MJS.

21st February, 1974.

Mrs. GRO-B
GRO-B
GRO-B

Dear Mrs. GRO-B

Thank you for bringing GRO-B up on Tuesday the 19th February.

I enclose a special Medical Card and confirm that he is now registered at this Haemophilia Centre. Dr. Ardeman agrees that you will be able to take him to Edgware General Hospital for treatment of minor problems, but I should like to know whenever he is needing treatment, so that I can keep a record. I am glad that GRO-B does not play rugby football and also that the soccer which he plays is entirely non-competitive. We usually advise people with mild haemophilia such as GRO-B that he is to lead an entirely normal life except that "contact body sports" such as rugger and boxing are forbidden. Ski-ing would also be rather inadvisable, should this question ever arise; violent football is not recommended either. I enclose a letter fo your own dentist. Please do not hesitate to get in touch if you have any problems.

Yours sincerely,

Katharine M. Dormandy

Enc.

THE HAEMOPHILIA CENTRE,

187,

Ext. GRO-C

KMD/MJS. 21st February, 1974.

Dr. S. Ardeman,
Consultant Haematologist,
Edgware General Hospital,
Edgware,
Middlesex.

Dear Dr. Ardeman,

re. GRO-B
GRO-B
d of b GRO-B 1959

This is to confirm that I have registered GRO-B and issued him with a special Medical Card. We made his factor VIII, 1%. As you say he has had remarkably little trouble and he obviously is mild, both clinically and from the laboratory point of view. Nevertheless he appears to have had a traumatic haemarthrosis of one knee when he was seven (they cannot remember which knee) and of the finger.

Mrs. GRO-B is anxious to be able to continue to come to Edgware General Hospital for cryoprecipitate for minor problems. She seems to know what she should do, but I am not quite clear. Perhaps, for my records, you could let me know sometime. Do they go to Casualty, or what is the arrangement?

As I have to make returns for the amount of cryoprecipitate used for each patient, together with the numbers of the bags given, would it be possible for you to do this and to let me have the appropriate information.

Yours sincerely,

Katharine M. Dormandy

Pond Street
Hampstead
London NW3 2QG

Telephone
01-794 0500
x GRO-C

The Royal Free Hospital

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT

IBK/VHL/ GRO-B

3 June 1987

not known by GP
letter received 24/6/87

Dr GRO-B

GRO-B

Dear Dr GRO-B

GRO-B GRO-B 99
GRO-B

Diagnosis Haemophilia A (Factor VIII:C - 5%)

I saw Mr GRO-B for his six monthly review in the Haemophilia Centre on 14 May 1987.

On examination his weight was 72.4 kg and blood pressure was 145/80. Pulse was 70 per minute. No lymphadenopathy was found. Chest was clear and cardiovascular system was clinically normal. Liver and spleen were not palpable. All joints had a full range of movement.

Investigations:

Haemoglobin	14.1 g/dl
Red Cell Count	5.06 x 10^{12}/l
White Cell Count	3.0 x 10^{9}/L
Platelets	182 x 10^{9}/l

His liver function tests and immunoglobulins were within the normal range. T lymphocyte subsets are just below the normal range.

In conclusion Mr GRO-B has not had any bleeding episodes over the last 6 months. He has been very well indeed. We will see him again in 6 month's time.

Yours sincerely

GRO-C

I B Kovacs MD PhD MRCPath
Haemophilia Centre

Pond Street
Hampstead
London NW3 2QG

Telephone
01-794 0500
EXT. GRO-C

The Royal Free Hospital

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT

KY/NK/ GRO-B

4th January 1988

Dr GRO-B
GRO-B
London GRO-B

Dear Dr GRO-B,

re: GRO-B dob GRO-B 59
GRO-B

Diagnosis - Haemophilia A 5%

I saw Mr GRO-B for his 6 monthly review early in December. He is well and has had no problems with bleeding. He last needed treatment in 1982. His general health is good. He eats well and has not lost any weight.

His weight is 71kg. Blood pressure 140/80. There was no lymphadenopathy. His chest is clear. His abdomen is soft and no masses are palpable. All joints had full range of movement.

Investigations: Hb 15.0g/dl, WBC 6.4×10^9/l, platelets 178×10^9/l. Renal and liver function tests and immunoglobulins are within the normal range. However, his T4 lymphocyte count has fallen since May 1987 from an absolute count of $.49 \times 10^9$/l to $.15 \times 10^9$/l. His T4 T8 ratio is 0.53. This is rather worrying and we will need to keep a close eye on him in the future. He will be reviewed in 6 months time, but I would stress that should GRO-B develop any illness or infections in the meantime, he should come up here to be seen immediately.

Yours sincerely

GRO-C

K L YONG MRCP
Haematology Registrar

Pond Street
Hampstead
London NW3 2QG

Telephone
01-794 0500

The Royal Free Hospital
Haemophilia Centre & Haemostasis Unit
Ext. GRO-C

SJ/NK/ GRO-B

21st July 1988

Dr GRO-B
GRO-B
GRO-B

Dear GRO-B

re: GRO-B dob GRO-B 59
GRO-B

Diagnosis: Haemophilia A Factor VIII 3%
HIV Positive

This 29-year-old man has been very well for the past six months working as the librarian in a drawing office. He has had no problems at all with his general health, apart from mild hayfever, and his haemophilia resulted in a bruised ankle during a ski-ing holiday, but he has had no other joint or bleeding problems. He is about to change jobs, and at the moment his new employer does not know about his haemophilia as there have been no direct questions asked about his health.

On examination, his weight is steady and he is generally well with no lymphadenopathy, his mouth is clear and the rest of his examination was unremarkable.

Investigations:

Full blood count normal apart from a neutropenia of 1.1.
Renal and Liver Function Tests normal.
T4 lymphocyte count 0.55, which is about the same as a year ago, and rather calls into question the result of .15 in December 1987. His anti HBS is negative, despite a booster in 1986 and I expect this reflects in his immuno competence.

I talked to GRO-B about the possibility of a trial of AZT in asymptomatic patients and said that we may write to him about it. Otherwise we plan to see him in six months time.

Yours sincerely

GRO-C

Sarah Janes
Haemophilia Registrar

Pond Street
Hampstead
London NW3 2QG

Telephone
01-794 0500
Ext GRO-C

The Royal Free Hospital

HAEMOPHILIA CENTRE AND HAEMOSTASIS UNIT

Dr P.B.A KERNOFF, MD FRCP MRCPath
Director
Dr CHRISTINE A LEE, MA MRCP MRCPath
Consultant Haematologist

SGL/LRB/

6th October 1988

Dear GRO-B

You may already know that the anti-viral drug AZT (zidovudine) has beneficial effects in AIDS patients and we have been using it for over a year in some of our patients.

The Medical Research Council has now approved a grant for study of the use of AZT in HIV infected people who are well or asymptomatic.

I have been appointed to organise and look after patients who enter this study. If you would like to discuss treatment with AZT or any aspect of the study with me or Dr. Christine Lee please contact us at the Haemophilia Centre. There is of course no obligation for you to enter the study even if you want to discuss it with one of us.

Yours sincerely,

GRO-C

Dr. S G Lim
Research Fellow

GRO-C

Dr. Christine Lee
Consultant Haematologist

Pond Street
Hampstead
London NW3 2QG

Telephone
01-794 0500
Ext GRO-C

The Royal Free Hospital

HAEMOPHILIA CENTRE AND HAEMOSTASIS UNIT

Dr P.B.A KERNOFF, MD FRCP MRCPath
Director
Dr CHRISTINE A LEE, MA MRCP MRCPath
Consultant Haematologist

CL/LRB/GRO-B

10th July 1989

Dr GRO-B
GRO-B
LONDON
GRO-B

Dear Dr GRO-B,

GRO-B GRO-B 59
GRO-B

This patient was seen on the 30th June for his six-monthly review. He is aged 29 and he sells marble. He has mild haemophilia with a factor VIII level of 5%. His last treatment was on the 12th January 1989 for a knee joint bleed. He acquired HIV probably in 1982 when he was treated with Armour Factor VIII and he is in the asymptomatic AZT trial.

On functional enquiry, he has been in very good health with no chest pain, indigestion or haematuria. He has had no arthropathy.

In the social situation, he rents a flat which he shares with two other men, they do not know that he is infected with HIV and neither do his parents. He has a brother who has not got haemophilia. A few close friends share the information about his HIV status.

On examination his mouth and skin were healthy, there was no lymphadenopathy, his chest was clear and his abdomen was normal.

INVESTIGATIONS:

Hb	13.6g/dl
Wbc	3.2 x 10^9/l
Platelets	178 x 10^9/l
I_A	30%
AST	19 iu/l

10th July 1989

CL/LRB/ GRO-B

GRO-B GRO-59

Thus there are no problems with this patient at present. I have however suggested that he discusses with our Social Worker the possibility of obtaining any help from the Mcfarlane Trust.

We will review him again in six months time.

Yours sincerely,

GRO-C

Dr Christine A Lee
Consultant Haematologist

Pond Street
Hampstead
London NW3 2QG

Telephone
071-794 0500
Ext. GRO-C

The Royal Free Hospital

HAEMOPHILIA CENTRE AND HAEMOSTASIS UNIT

Dr P. B. A. KERNOFF, MD FRCP MRCPath
Director
Dr CHRISTINE A. LEE, MA MD FRCP MRCPath
Consultant Haematologist

CL/LRB/ GRO-B

13th December 1990

Dr GRO-B
GRO-B
LONDON
GRO-B

Dear Dr GRO-B

GRO-B GRO-B 59
GRO-B

This 30 year old man who works as a manager of a warehouse and has moderate haemophilia A came for his annual review on the 12th December. He has had no bleeds during the past year. It is probable that he seroconverted in November 1982 when he received unheated factor VIII for treatment of a cut finger. He is completely asymptomatic as far as his HIV disease is concerned and is running a CD4 count of about 0.5. He is in the Concorde Trial which compares zidovudine with placebo and he started this on the 12th January 1989.

I had a long discussion with him about the various treatments of HIV. He is engaged to a secretary and he has seen Mrs Miller, our Medical Social Worker and AIDS Counsellor to discuss this impending marriage and he brought his girlfriend along with him. She has been tested and will be tested again in March.

On examination his weight was 73.9kgs, there was no lymphadenopathy, his mouth was healthy, he did have some scaling leisons on his left hand and arm, his chest was clear and in the abdomen there were no masses.

CL/LRB/ GRO-B

13th December 1990

GRO-B GRO-B 59

INVESTIGATIONS:

12.12.90

Haemoglobin	13.5 g/dl
White Blood Count	3.0 x 10^9/l
Platelets	176 x 10^9/l
CD4 Count	0.27 x 10^9/l
AST	28 iu/l

He will be seen in three months time as follow-up of his Concorde trial and we will see him in a years time for his annual review.

Yours sincerely,

GRO-C

Dr Christine A Lee
Consultant Haematologist

GRO-C

Dr. GRO-C

28.1.91
10.10am

31-5-91
9.30

Pond Street 4/12/90
Hampstead
London NW3 2QG

Telephone
071-794 0500
Ext. GRO-C

The Royal Free Hospital

HAEMOPHILIA CENTRE AND HAEMOSTASIS UNIT

Dr P. B. A. KERNOFF, MD FRCP MRCPath
Director
Dr CHRISTINE A. LEE, MA MD FRCP MRCPath
Consultant Haematologist

CL/LRB/ GRO-B

13th December 1990

Dr Malcolm Rustin
Consultant
Dept. of Dermatology
RFH

Dear Malcolm,

GRO-B GRO-B 59
GRO-B

I would be grateful if you would send an appointment to see this 31 year old patient who has moderate haemophilia A but has become infected with HIV. At the present time he is asymptomatic as far as his HIV and he has a CD4 count running at about 0.5. His complaint is that he has a dermatitis, particularly of his left hand which he attributes to handling marble in his work, he is a manager of a warehouse.

I think that in the past he has been prescribed hydrocortisone which he says has helped, but I thought that it would be important for him to see a Dermatologist for your advice regarding management. He is expecting to hear from you.

Yours sincerely,

GRO-C

Dr Christine A Lee
Consultant Haematologist

Pond Street
Hampstead
London NW3 2QG

Telephone
071-794 0500
Ext.

The Royal Free Hospital

HAEMOPHILIA CENTRE AND HAEMOSTASIS UNIT

Dr P. B. A. KERNOFF, MD FRCP FRCPath
Director
Dr CHRISTINE A. LEE, MA MD FRCP MRCPath
Consultant Haematologist

CAL/LRB/ GRO-B

19th March 1991

Dr GRO-B
GRO-B
LONDON
GRO-B

Dear Dr GRO-B,

GRO-B GRO-B 59
GRO-B

This patient came for follow-up of the Concorde trial on the 15th March. He has probably been infected with HIV since 1982 but he only has mild haemophilia. He is well apart from a dermatitis on his hands which is thought to be work-related and possibly a wart on his lower lip. I am going to refer him to the Dermatologists for this.

He brought his girlfriend with him, GRO-B because they are planning to get married in GRO-B and we had a long discussion about their sexual relationship, having children and their relationship with her parents and telling her about GRO-B 's HIV and haemophilia. I am going to see them again on the 10th May.

On examination he was healthy apart from the dermatitis on his hands and a lesion on the lower lip which looks like a wart, but I will ask for a dermatological opinion. He remains on a thousand milligrams of zidovudine or placebo daily and the CD4 count today, the 15th March, was 0.38 x 10^9/l. He will be reviewed again in three months time.

Yours sincerely,

GRO-C

Dr Christine A Lee
Consultant Haematologist

The Royal Free Hampstead
NHS Trust

Pond Street
Hampstead
London NW3 2QG

Telephone
071-794 0500
Ext.

HAEMOPHILIA CENTRE AND HAEMOSTASIS UNIT

Dr P. B. A. KERNOFF, MD FRCP FRCPath
Director
Dr CHRISTINE A. LEE, MA MD FRCP MRCPath
Consultant Haematologist

CAL/MJ/ GRO-B

PRIVATE AND CONFIDENTIAL

19 June 1991

TO WHOM IT MAY CONCERN

Re: GRO-B GRO-B 59
GRO-B

This is to confirm that this patient has mild haemophilia A and is also infected with HIV as a result of factor VIII treatment in the past.

At the present time, he is completely well and asymptomatic. He has an extremely good and normal immunity as measured by the CD4 count at the present time. I would not expect him to become ill on the account of HIV infection whilst in the United States of America.

Yours sincerely

GRO-C

Christine A Lee
Acting Director

CC Liz Boyd
Haem Centre

Pond Street
Hampstead
London NW3 2QG

Telephone
071-794 0500
Ext.

The Royal Free Hospital

HAEMOPHILIA CENTRE AND HAEMOSTASIS UNIT

Dr P. B. A. KERNOFF, MD FRCP FRCPath
Director

Dr CHRISTINE A. LEE, MA MD FRCP MRCPath
Consultant Haematologist

25th June 1991

Mr. David Rollman
VCU
US Embassy
[illegible] osvenor Square
[illegible] ndon W1

Dear Mr. Rollman,

re : GRO-B DOB GRO-B9
GRO-B

I am writing to you with regards to this young HIV positive haemophiliac who contracted HIV from contaminated factor VIII infusions. He is getting married on the GRO-B this year and intends going to Florida for his honeymoon. Unfortunately, this was only a late decision and he also did not realize that a waiver was needed till recently. He is a mild haemophiliac and normally uses factor VIII infrequently, but is perfectly capable of self-treatment. He is currently in the asymptomatic phase of HIV infection and the only medication he is receiving is AZT trial capsules. I do not envisage him to develop any medical problems arising out of his HIV for the two weeks he intends to stay in [illegible] lorida (from July 14th onwards). I hope that you will consider his application [illegible] or a waiver favourably and expedite the application in view of the short time available.

yours sincerely,

GRO-C

Dr. Seng Lim
MRC Research Fellow
Haemophilia Centre
Royal Free Hospital

Pond Street
Hampstead
London NW3 2QG

Telephone
01-794 0500

The Royal Free Hospital

CMV RESULT

28 January 1992

The CMV status in 1988 of GRO-B was negative. (Immunoglobulin G antibodies)

Christine A Lee

ROYAL FREE HOSPITAL
POND STREET
LONDON NW3 2QG
TELEPHONE 071 794 0500

THE ROYAL FREE HAMPSTEAD
Royal Free Hospital
NHS TRUST

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
FAX No: 071 431 8276

Director: Dr Christine A Lee MA MD MRCPath FRCP

PT/LRB: GRO-B

16 July 1992

Mr GRO-B
GRO-B
GRO-B
GRO-B

Dear Mr GRO-B

I am enclosing a letter from the Concorde Trial Centre. You may know that the trial results up to April 1992 were independently analyzed by the Data and Safety Monitoring Committee, and their conclusion was that we should continue the trial until March 1993. In some ways it is frustrating not to have an answer yet, but hopefully in a further nine months we will have a significant result to answer the important question of whether to use AZT at an early stage of infection.

We are all very grateful to you for participating in the trial up until now, and I hope that you will feel able to continue until March 1993. If you would like to discuss this further with myself or Dr Lee, please do not hesitate to get in touch.

Yours sincerely,

GRO-C

Dr Paul Telfer
Registrar in Haemophilia

enc.

PT/CRAMOND CTC

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LONDON NW3 2QG

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Royal Free Hospital
NHS TRUST

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
FAX NO: 071 431 8276

Director: Dr Christine A Lee MA MD MRCPath FRCP

PT/LRB: GRO-B

8 March 1993

Dr GRO-B
GRO-B
LONDON GRO-B

Dear Dr GRO-B

Re: GRO-B GRO-B 59

Diagnosis: Mild Haemophilia A
HIV seropositive

Trial: Concorde trial

This patient attended for routine trial follow up.

Comments:

Yours sincerely,

GRO-C

Dr Paul Telfer
Research Registrar

ROYAL FREE HOSPITAL
POND STREET
LONDON NW3 2QG

TELEPHONE 071 794 0500

THE ROYAL FREE HAMPSTEAD
Royal Free Hospital
NHS TRUST

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
Director: Dr Christine A Lee MA MD MRCPath FRCP

TEL NO: GRO-C
FAX NO:

PT/LRB GRO-B

29 March 1993

Mr GRO-B
GRO-B
GRO-B
GRO-B

Dear Mr GRO-B GRO-B

We are organising a patients' meeting on Wednesday 28th April at 8 pm in the Haemophilia Centre Seminar Room at the Royal Free Hospital.

This will be an opportunity to discuss current advances in the understanding of HIV infection, and new forms of therapy treatment being developed. In particular, we hope that we will be able to present the results of the Concorde trial, which investigated the use of AZT early in the course of HIV infection.

Please could you fill in and return the reply slip below. I should mention, that parking is likely to be difficult because of building work going on adjacent to the Haemophilia Centre and the most likely site to obtain a place will be in the car park at the main hospital entrance in Pond Street.

Yours sincerely,

GRO-C

Dr Paul Telfer

.....

I will/will not be attending the patients meeting at 8 pm on 28th April 1993.

I will be bringing ..... guest(s).

ROYAL FREE HOSPITAL
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Royal Free Hospital
NHS TRUST

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
Director: Dr Christine A Lee MA MD MRCPath FRCP
TEL NO:
FAX NO: GRO-C

AT/LRB/ GRO-B

14 June 1993

To whom it may concern

Dear Doctor,

GRO-B GRO-B 59
GRO-B

Diagnosis: Moderate Haemophilia A - Factor VIII 5%
HIV antibody positive

Mr GRO-B had his annual review on 7th June 1993. He has had no bleeds during the past year. He did not have any dental problems, neither joint problems. He is completely asymptomatic as far has his HIV is concerned and his past CD4 count done on 8th March 1993 was 0.35. He is now off the concorde trial.

His general health is good. His weight is 74.1 kg. There was no lymphadenopathy. His mouth was healthy with no thrush. He did not have any skin lesions. The abdomen was soft with no hepatosplenomegaly. His chest and heart examination were normal. His joint examination was also normal. Blood for review was taken. We will see him in a years time and he will continue to see Dr Paul Telfer for other trials.

Yours sincerely,

GRO-C

Dr Ali Taheri

AT/LRB/DARLINGTON

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LONDON NW3 2QG

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THE ROYAL FREE HAMPSTEAD
Royal Free Hospital
NHS TRUST

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
Director: Dr Christine A Lee MA MD FRCP FRCPath
Consultant: Dr K John Pasi MB MRCP MRCPath

TEL NO:
Fax No: GRO-C

Out of hours: GRO-C

Dr GRO-B

GRO-B

MIDDX GRO-B

Dear Dr GRO-B

Re: GRO-B

Diagnosis: Haemophilia A

This patient attended the Haemophilia Centre today. 5 4 94

Problem:

Action:

Comments: Family Counselling

Yours sincerely,

GRO-C

Christine Lee

GRO-C

John Pasi

c:\BLINDA\WP\PASI\MISC\DIAG

ROYAL FREE HOSPITAL
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TEL No: GRO-C
Fax No: GRO-C
Out of hours: GRO-C

PT/LRB/ GRO-B

21 June 1994

Dr GRO-B
GRO-B
Middx GRO-B

Dear Dr GRO-B

GRO-B GRO-B59
GRO-B

GRO-B was seen with his wife GRO- in the Haemophilia Centre on the 20th June for a review visit. He is very well in himself and has had no bleeding problems for several years now. Both he and his wife have a good knowledge of haemophilia and its treatment. However, GRO-B did not have a greencard and was not aware of the arrangements for urgent treatment out of hours, should they be required. This has been rectified. We discussed HIV infection. In his case, the clinical markers would suggest that he is not progressing rapidly. The most recent CD4 count, in March of this year, was 460 cells/cubic mm. He did report very occasional night sweats, but I don't believe these are significant. His wife is now 14 weeks pregnant and is currently well. We have arranged repeat viral serology tests to be done today.

On examination there were no abnormal physical signs. GRO-B's weight was 75.7 kg. He will be reviewed in three months' time.

Yours sincerely,

GRO-C

Dr Paul Telfer
Research Registrar in Haemophilia

GRO-B

ROYAL FREE HOSPITAL
POND STREET
LONDON NW3 2QG

TELEPHONE 071 794 0500

THE ROYAL FREE HAMPSTEAD
Royal Free Hospital
NHS TRUST

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
Director: Dr Christine A Lee MA MD FRCP FRCPath
Consultant: Dr K John Pasi MB MRCP MRCPath

TEL NO: GRO-C
Fax No:

Out of hours: 071 794 0500 bleep 813

Dr GRO-B
GRO-B
GRO-B MIDX GRO-B

Dear Dr, GRO-B

Re: GRO-B

Diagnosis:

This patient attended the Haemophilia Centre today. 13-9-94

Problem: Reviewed via ?

Action:

Comments:

Yours sincerely,

GRO-C
Christine Lee

GRO-C
John Pasi

c:\BLINDA\WP\PAST\MISC\DIAG

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
Director: Dr Christine A Lee MA MD FRCP FRCPath
Consultant: Dr K John Pasi MB PhD MRCP MRCPath
Senior Lecturer: Dr David J Perry MD PhD MRCP MRCPath

Tele No: GRO-C
Fax No:

CAL/sh

This patient GRO-B was in the Concorde trial

number GRO-B

He was treated with Placebo

GRO-C

Christine Lee
December 1994

ROYAL FREE HOSPITAL
POND STREET
LONDON NW3 2QG
TELEPHONE 0171 794 0500

THE ROYAL FREE HAMPSTEAD
Royal Free Hospital
NHS TRUST

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
Director: Dr Christine A Lee MA MD FRCP FRCPath
Consultant: Dr K John Pasi MB PhD MRCP MRCPath
Senior Lecturer: Dr David J Perry MD PhD MRCP MRCPath
Tele No: [redacted]
Fax No: GRO-C

KJP/KB/ GRO-B

7 June 1995

Dr GRO-B
GRO-B
Middlesex
GRO-B

Dear Dr GRO-B

Re: GRO-B DoB GRO-B 59
GRO-B

This gentleman, with mild haemophilia A, came up to the Centre today for a review. It is quite a while since he had a review. He has not required much treatment with regard to his haemophilia apart from a recent elbow injury when he fell off his bike. Other than that injury he has only had one other need for treatment over the last year which is when he had an injury to his hand. Treatment is usually given at the Royal Free Haemophilia Centre. With regard to his general health, this is at the moment quite good. His weight is stable if not increasing and he has no other particular symptoms of note other than some dermatitis and tinea in his toe spaces.

Examination was essentially unrevealing apart from a resolving haematoma over the point of his right elbow.

Routine investigations have recently shown normal liver function tests, normal full blood count, hepatitis B surface antibody negative (non-responder), hepatitis C antibody negative, CD4 count 0.31 x 10^9/l, P24 antigen positive < 25 pg/ml.

In essence GRO-B is actually very well at present and there are no major issues. His CD4 count is well above that at which we would start prophylactic drug medication. We will see him again for review in 3-6 months time.

Yours sincerely

GRO-C

John Pasi

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Consultant: Dr K John Pasi MB PhD MRCP MRCPath
Senior Lecturer: Dr David J Perry MD PhD MRCP MRCPath

CAL/MJ/215710

22 September 1995

Mr GRO-B
GRO-B
GRO-B
GRO-B
GRO-B

Dear GRO-B

We would like to invite you to come the Haemophilia Centre to discuss the possibility of you being entered into a new study conducted by the Medical Research Council. This "Quattro Trial" is special in the sense that it is directed towards a small group of patients at seven hospitals in London who have had no antiviral therapy. It is an open-label study so you will know exactly what medications you will be taking and there is no placebo drug.

This is a study that is comparing the effects of four (4) antiretroviral drugs (old as well as new ones) either given concurrently or cyclically.

There are only eight (8) of you from our centre eligible to enter this study, so please do take this opportunity and give us a call to make an appointment to see either Dr Lee or myself.

With best wishes.

GRO-C

Dr Thynn Thynn Yee MRCP
Research Fellow

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KJP/KB/ GRO-B

16 July 1996

Dr GRO-B

GRO-B

GRO-B

Dear Dr GRO-B

Re: GRO-B DoB GRO-B 59
GRO-B

This man was recently seen in the Haemophilia Centre by one of the Registrars when he presented with abdominal pain. I gather that you have not had a letter concerning this event in May, and hence this letter.

From the notes it would appear that he presented with abdominal pain and he subsequently was endoscoped and found to have mild duodenitis. A breath test showed that he was negative for H.Pylori infection. As a result he has been started on 150 mg of ranitidine on a twice daily basis. The follow-up ultrasound that was performed in June showed that there was no other alternative probable cause for his abdominal pain. He should therefore continue for the foreseeable future on ranitidine at the dose listed above.

Yours sincerely

GRO-C

John Pasi

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CAL/MJ

13 August 1996

Private and Confidential

Ms Chloe Beer
Clerical Assistant
The Macfarlane Trust
PO Box 627
London SW1H 0QG

Dear Ms Beer

GRO-B GRO-B 59

This man has severe haemophilia A. He is also infected with HIV and HCV. His last CD4 count is May of this year, was 380 per μl. He is therefore, not on any medication at the present time but, he recently has had a problem with mild duodenitis for which he had endoscopy but, was found to be H pylori negative.

Yours sincerely

GRO-C

Christine A Lee

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KJP/KB/ GRO-B

25 February 1997

Dr GRO-B
GRO-B
Middlesex
GRO-B

Dear Dr GRO-B

Re: GRO-B DoB GRO-B 59
GRO-B

This man with mild haemophilia A came up to the Centre today for follow-up. It is quite a considerable while since he was reviewed in the Centre. Fortunately he has only required treatment twice in the last two years, once prior to an endoscopy and once after a thumb injury. Indeed we have not seen him on any other occasion since and hence the lack of correspondence from us about his problems.

It is fortunate that GRO-B has not had any bleeding complications and we continue to treat him on demand if he has any injuries or bleeding problems. His GI symptoms have largely resolved on intermittent courses of ranitidine. He has now been off ranitidine for a month and has no symptoms. If he gets a recurrence of his symptoms I have suggested a repeat six month course.

He remains well from his HIV, although when previously tested he has continued to be shown to be P24 antigen positive. His last CD4 count at the beginning of January was 0.28 x 10^9/l. He has no symptoms attributable to progressive HIV disease. Interestingly we have found that he is HCV PCR negative.

GRO-B is clearly doing reasonably well from his HIV disease. His recent blood tests were all quite encouraging. However, his main problem at the moment that he feels is significant is intermittent bouts of depression. He has seen our Counsellor Mrs Riva Miller today to approach this. We would be quite happy to refer him on for psychiatric professional support if this is appropriate and if he wishes to seek this type of support. We have left this issue with him at the moment and he will get back to us on this specific point.

continued...

25 February 1997

I am sure we will probably be seeing GRO-B before his next six monthly appointment because of his present problem with depression but otherwise we would plan to see him again in six months as mentioned.

Yours sincerely

GRO-C

John Pasi

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DJP/LRB GRO-B

26 September 1997

Mr GRO-B
GRO-B
GRO-B
GRO-B
GRO-B

Dear Mr GRO-B

We would like to invite you to participate in a clinical trial of antiretroviral therapy conducted by the Medical Research Council, called the '*ProCom*'. **All** participants in this trial will be receiving a **four** drug combination consisting of 2 protease inhibitors and 2 reverse transcriptase for the **first 16 weeks** and then will be randomised as follows:

1. Some will continue with the 4 drug combination for another 64 weeks.

2. Some will carry on with the 2 protease inhibitors only for another 64 weeks.

3. Some will continue with the 2 reverse transcriptase only for another 64 weeks.

This is clearly a very good clinical trial and will include 200 patients in the UK. I have enclosed a patient information sheet for you to read through and if you are interested in taking part or need further information you can ring up the Haemophilia Centre at the Royal Free Hospital and get an appointment to see Professor Christine Lee or myself for discussion.

Yours sincerely,

Dr Thynn Th GRO-C
Clinical Rese

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KJP/KB/ GRO-B

6 November 1997
Clinic: 5 November 1997

Professor C A Lee
Director
Haemophilia Centre
RFH

Dear Christine

Re: GRO-B **DoB** GRO-B 59
GRO-B

I would be grateful if it would be possible for you to see GRO-B in one of your review clinics to consider his HIV disease and anti-HIV therapy. As you know GRO-B has had fairly well preserved CD4 counts with the last count that we have in January of 0.28 x 10^9/l. We are awaiting his recent result from this visit. He has been quantitated at over 100,000 copies/ml HIV. He is quite well at the moment. I think he would very much appreciate the opportunity to consider how the field of HIV therapy has moved on.

I have arranged for his repeat CD4 to be performed and also a repeat HIV quantitation which I hope will be ready fairly soon. I have not given him an appointment and said that we would be in touch in due course.

Many thanks.

GRO-C

Kind regards.

Yours sincerely

GRO-C

John Pasi

Viral load 123,000 6/11/97
5.09 log

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CAL/ML

2 December 1997

Mr GRO-B

GRO-B

Dear Mr GRO-B

It is our practice to keep you informed of issues that relate to haemophilia care. You may have heard or read about CJD and the concerns that the agent causing this may be transmitted by blood transfusion and blood products. **At the present time there is no evidence for this.** The basis for scientific speculation is that the new form of CJD (new variant CJD) infects the lymphocytes, a type of white cells which are found in the blood. Blood products used for the treatment of inherited bleeding disorders do not contain white cells.

As a consequence of these concerns, and as a precautionary measure, there have been two recent recalls of BPL Factor VIII batches because it was found that "a donor had not met the current health requirements for CJD".

According to our records, you received some of the Replenate batch FHE4548 in the past.

What is known about the transmission of new variant CJD to humans is that it has probably arisen from ingestion of beef products containing the agent responsible for BSE in cattle. The medical and scientific issues are complex. We will ensure that we keep them under close review, as new information becomes available, so that we may keep you fully informed. In the meantime, if you have any concerns you wish to discuss, in the first instance please contact one of the nurses at the Centre on 0171 830 2557.
If you wish to discuss these issues in person, please ask for an appointment with one of us, the consultant medical staff.

Yours sincerely

GRO-C
Professor Christine Lee

GRO-C
Dr John Pasi

GRO-C
Dr David Perry

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KJP/KB/ GRO-B

16 June 1998

Dr GRO-B
GRO-B
Middlesex
GRO-B

Dear Dr GRO-B

Re: GRO-B DoB GRO-B 59
GRO-B

I reviewed GRO-B in our Haemophilia Centre on GRO-B 98. He had stood on a rusty nail at home while gardening. The nail had penetrated and on examination there was an obvious entry site with some bruising around the area. We therefore cleaned the puncture site in our clinic today and treated GRO-B with factor VIII, both for the injury and for his tetanus toxoid booster which we gave today. He will return should he have any problems.

Yours sincerely

GRO-C

Dr Karen Murphy
Specialist Registrar in Haematology

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CAL/ML GRO-B

24/06/98

Dr GRO-B
GRO-B
Middx GRO-B

Dear Dr GRO-B

Re GRO-B GRO-B 59)
GRO-B

I saw this 38 year-old man on the 23rd of June. He has factor VIII deficiency with a level of 3 u/dl. He works in a GRO-B shop and he came with his wife and I saw him together with Mrs Miller, our Social Worker. He is infected with HIV, but he appears to have cleared hepatitis C and is PCR negative. He was last treated with factor VIII for an ankle in November 1997. He is able to treat himself, although he only rarely needs treatment.

On functional enquiry, he remains on Ranitidine, having been diagnosed as a small erosion in May 1996. He is otherwise well. His most recent problem was that he trod on a nail and had a tetanus boaster on the 12th of June. He had an HIV viral load measured in March 1996 which showed a level of 95,400 with a CD4 count of 259.

I think he really should be treated with triple therapy and I have advised that. However, in the process of discussing this, he said that he wants to have another baby. Clearly, if he was thinking of conceiving it would not be a good idea to put him on anti-viral therapy. I said that I would refer him to Dr Johnson for advice in the meantime whilst he and his wife are considering this issue.

GRO-B

He has been consistently PCR negative for hepatitis C and has normal transaminases. It looks as if he has cleared this virus. He has also lost his antibody to hepatitis A and B.

His wife GRO-B works in the Community looking after psychiatry patients. She is a GRO-B They have one child GRO-B aged 3½. Apparently, this pregnancy was achieved easily, having only taken two risks of unprotected sex mid cycle. However, his wife says that the delivery was difficult in that she had an emergency Caesarean section and the child was on the Intensive Care on a ventilator after the birth. We went through all the issues and risks around a pregnancy where the putative father is infected with HIV and the risks of infection. We also suggested that there is a problem about the high HIV viral load which might make HIV transmission easier. He and his wife are going to think on this issue further, and in the meantime, they will be reviewed in Dr Johnson's clinic and I will see them again in approximately 3 weeks.

Yours sincerely

GRO-C

Christine A Lee
Professor of Haemophilia

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THE ROYAL FREE HAMPSTEAD N.H.S. TRUST
Royal Free Hospital
LAWN ROAD DIVISION

11 AUG 1998

DEPARTMENT OF THORACIC MEDICINE

Tel: GRO-C **fax** GRO-C
e.mail: mjohnson@ GRO-C

Our Ref: MAJ/SA

GRO-C

10th August 1998

Professor C A Lee
Professor of Haemophilia
Department of Haemophilia
Royal Free Hospital

Dear Christine,

RE: GRO-B **DOB** GRO-B 59 - GRO-B
GRO-B

Thank you for asking me to see this patient. He tells me he has been HIV positive probably since the early 1980's and has never required any therapy. However recently his CD4 has been falling and is now 0.121 x 10^9/l and his viral load is >750,000 copies/ml. However he remains well with good health and no specific symptoms. In view of his lack of progression he has never really considered antiviral therapy until recently and now is quite settled about starting treatment but wanted to discuss the timing of this as he and his wife would like to consider a further pregnancy. They have one 3 and a half year old child and they would like to use his semen and know the risks of possible HIV transmission. They wanted to discuss whether there would be any evidence of toxicity in terms of the sperm from antiviral treatment and I told them that I thought that this was unlikely but that if he had started on antiviral treatment and the viral load was low, that it was probable that the risk of her being infected would be less.

Continued/...

RE: GRO-B - DOB GRO-B 59 - GRO-B
GRO-B

Following this discussion they decided that he would like to start on antiviral treatment. I wondered whether a combination of Combivir with Nelfinavir 1250 mgs b.d. might be a reasonable option given that Ritonavir at present is not available in the capsule form. I have discussed this with them and they will come back to see you in the near future to discuss further management.

With best wishes.

Yours sincerely,

GRO-C

Dr M A Johnson, MD, FRCP
Consultant Physician in Thoracic Medicine/HIV/AIDS

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CAL/ML

28/08/98

Dr GRO-B
GRO-B
Middx GRO-B

Dear Dr GRO-B

Re GRO-B GRO-59)
GRO-B

I saw this patient on the 25th of August to start his anti-HIV treatment which has been recommended by Dr Johnson. He has been started on Combivir bd which is 300 mg of Zidovudine bd combined with 150 mg of 3TC and Nelfinavir 1250 mg bd. At the present time, there are no plans for his partner to get pregnant and the strategy is to try and reduce his HIV viral load.

I have advised that he gets a drug season ticket to ease the expense of all these.

Yours sincerely

GRO-C

Christine A Lee
Professor of Haemophilia

cc Mrs Liz Boyd

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CAL/MJ GRO-B

2 October 1998

Dr GRO-B
GRO-B
Middx GRO-B

Dear Dr GRO-B

GRO-B GRO-B 59
GRO-B

I saw this patient today, 30th September. He is due to start anti-HIV treatment with combivir 300 mg of zidovudine bd and 3TC 150 mg bd, together with nelfinavir 1250 mg bd. However because of delay in getting these prescription drugs, he has not started treatment yet.

He was complaining of some folliculitis, for which I have prescribed trimovate cream and also of an infected lesion round his nail bed of the right big toenail. Because of a possible allergy to penicillin, he has been prescribed erythromycin. I suggested that he starts taking his anti-HIV drugs after he has completed the five day course of antibiotics.

Yours sincerely

GRO-C

Christine Lee
Professor of Haemophilia

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CAL/MJ/ GRO-B

17 February 1999

Dr GRO-B
GRO-B
Middx GRO-B

Dear Dr GRO-B

GRO-B GRO-B 59
GRO-B

I saw this patient, who has mild haemophilia A with a factor VIII of 5 u/dl, on 10th February for his review. He is now aged 39 and works in a health food store. He acquired HIV infection in 1982, at the time of an injury to his hand. He was last treated with factor VIII in November 1987 for an ankle joint.

He started treatment in mid-October 1998 with combivir (300 mg zidovudine, 150 mg 3TC) bd and nelfinavir 1250 mg bd. However, he said that he only took these drugs erratically during the following six weeks because they caused nausea. He did find that while he was on them, his rash completely cleared up. He has had no medication since the end of November, but he would like to restart this now.

He has lost his antibody to hepatitis A, he has lost his antibody to hepatitis B. He was infected with hepatitis C in 1982 and we have had one recent PCR-negative result in January 1997, but he recorded a viral load of $1x10^6$ on 23rd June '97. Quite clearly, he has a low viral load and he has normal transaminases so for the present, he needs no intervention with regard to this hepatitis C.

His relationship with his partner GRO-B going well, although he is not planning a pregnancy at the present time – he has a son GRO-B aged 4.

On examination, he has widespread seborrhoeic dermatitis, which I am sure will get better if he manages to take his anti-HIV viral medication and get immune reconstitution. In the meantime, I have prescribed trimovate cream.

I will review him in a month's time and I have given him a prescription for zidovudine, 3TC and nelfinavir.

Yours sincerely

GRO-C

Christine Lee
Professor of Haemophilia

GRO-B

MIH01
27/9/99
10-00

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CAL/MJ/ GRO-B

06 May 1999

MIH01
MIH03
MI - 5
4 8
GENT

Dr. M. I. Hamilton
GASTROENTEROLOGY
Received 7/5/99

Dr Mark Hamilton
Department of Medicine
RFH

Dear Mark

GRO-B GRO-B 59
GRO-B

I would be grateful if you would see this 39 year old man, who has mild haemophilia A and is co-infected with HIV and hepatitis C. He is on triple therapy for his HIV, with zidovudine, 3TC and nelfinavir.

He was complaining of upper abdominal discomfort when he came to see me on 4th May. He has this particularly at night, particularly when he has eaten late. I note that he was found to be antibody negative for helicobacter pyelori in 1994. He had an endoscopy in May '96, which showed a pyeloric erosion and he was started on treatment with ranitidine. It would appear that it was the intention for him to have a breath test, but I cannot see any evidence of this. Since 1996, he has taken ranitidine erratically and is not on it at present.

I would be very grateful if you would review his abdominal symptoms and reconsider the necessity, or otherwise, of endoscopy and breath test etc. He is expecting you to send him an appointment directly.

Yours sincerely

GRO-C

Christine Lee
Professor of Haemophilia

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Royal Free Hospital
GRAY'S INN DIVISION

UNIVERSITY DEPARTMENT OF MEDICINE

MH/LK/ GRO-B
clinic: 27/9/99
8 October 1999

GRO-C

Professor Christine Lee
Professor of Haemophilia
Royal Free Hospital

Dear Christine

GRO-B, d GRO-B 59
GRO-B

Thank you for asking me to see this 39 year old man who complains of dyspepsia. He has increased symptoms over the last few months which have been helped partially by Zantac but which he last took some 18 months ago. He notices low back discomfort which may cause nausea and vomitting. I note that he has had some night-time discomfort although recently he has not been waking at night and that certain foods may trigger the discomfort. He has occasional heart burn and I note that he is no highly active anti-retro viral therapy but no current anti-secretory therapy.

On general examination he looked without lymphadenopathy or anaemia. His abdomen was soft but with some tenderness in the right upper quadrant and epigastrum. I think this man with recurring H2 receptor antangonists responsive dyspepsia merits further investigation. As I gather a breath test has been previously negative, I have arranged for an upper GI endoscopy to investigate further.

Yours sincerely,

GRO-C

Dr Mark Hamilton MB (Hons) MD MRCP
Consultant Physician and Gastroenterologist

Dr GRO-B
GRO-B

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CAL/alb/ GRO-B

20th October 1999

Dr GRO-B

GRO-B

Middx

Dear Dr GRO-B

GRO-B D.O.B GRO-B 59
GRO-B

I saw this 40 year old man on the 19th October for review. He has haemophilia A with a factor VIII of 5 u/dl (normal range 50-150). He is infected with both HIV and HCV. He was last treated in 1997 for an ankle bleed. He is currently undergoing investigation for abdominal discomfort. He was originally found to be helicobacter pylori antibody negative in 1994. He had an endoscopy in May 1996, when a pyloric erosion was found and he was treated with ranitidine. He is now being reviewed by Dr Hamilton and is due to have an endoscopy on Friday 22nd October under Factor VIII cover.

He is infected with HIV; the last viral load we have on record was 149 000 on 4th May with a CD4 count of 58/microlitre. He has been on triple therapy with Combivir, 300 mg Zidovudine b.d. and 150 mg sTC b.d., and Nelfinavir 1250 mg b.d. It is possible that he is not taking all his drugs, and we will check his CD4 count and HIV viral load. It may be that we will have to refer him to Dr Johnson's clinic.

Continued/2..

He is HCV negative and HVB negative. He has a very low hepatitis C viral load of .6 x 10^6 with normal transaminases.

He still continues to work in his health food shop, but he is shortly to be moving to Bedford, although he will continue this work.

Thus, in conclusion, we need to review the response to his HIV drugs and possibly refer him to the joint HIV clinic with Dr Johnson, and we continue to investigate his GI symptoms. I will see him again in six months for a review.

Yours sincerely

GRO-C

Christine Lee
Professor of Haemophilia

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Senior Lecturer: Dr David J Perry MD PhD FRCP FRCPath
Consultant: Dr Simon A Brown MB MRCP MRCPath
Tele
Fax GRO-C

BW/kb

7 December 1999

Mr GRO-B
GRO-B
GRO-B
GRO-B
GRO-B

Dear Mr GRO-B

It is the policy of our Haemophilia Centre to update services for patients in line with recent advances in haemophilia care. It is now possible to identify the genetic abnormality responsible for most cases of haemophilia A. The identification of the specific problem that has resulted in you developing haemophilia will allow a better understanding of haemophilia. It will also allow us to develop a rapid and accurate test for detecting whether female members of your family are carriers of the haemophilia gene.

We have currently limited funding to carry out this test and therefore if you wish to be tested you should ideally be seen before the end of March 2000. Dr Barry White is a clinical fellow at the Haemophilia Centre and will be working with Sister Chris Harrington and Mrs Riva Miller to ensure that everyone has the opportunity to be tested.

I hope very much that you will make an appointment to come and discuss this test. If you are agreeable a blood sample will be taken at the same visit. Appointments can be made by ringing the Haemophilia Centre at 0171 830 2068 and arranging to see Dr Barry White on a Monday or Tuesday afternoon between 2 and 4 pm. We would be grateful if you could inform us, by contacting the same number, if you do not wish or are unable to attend.

Please contact Dr White by ringing the above number if you have any questions regarding this matter.

Yours sincerely

GRO-C
Christine Lee

GRO-C

GRO-C
Simon Brown

ROYAL FREE HOSPITAL
POND STREET
LONDON NW3 2QG

TELEPHONE 020 7794 0500

THE ROYAL FREE HAMPSTEAD
Royal Free Hospital
NHS TRUST

THE HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT TEL: GRO-C
Director: Professor Christine A Lee MA MD DSc(Med) FRCP FRCPath FAX
Senior Lecturer: Dr David J Perry MD PhD FRCP FRCPath Out of hours: 0207 794 0500
Consultant: Dr Simon A Brown MB MRCP MRCPath

MJ/gs/GRO-B/9th January 2000

GP: Dr GRO-B
GRO-B
Middlesex

Dear Dr GRO-B,

Patient: GRO-B GRO-B DO GRO-B 59
GRO-B

Special Combined – 9th January 2001
Consultants: Dr Margaret Johnson - Consultant Physician
Professor Christine Lee - Consultant Haematologist

We reviewed Mr GRO-B in the Combined HIV/Haemophilia Clinic on 9th January 2001. From an HIV point of view, he is well. He has had no problems and has been very compliant with his drugs. The only side-effect is that he does have some diarrhea some of the time. However, his appetite is good and he has not lost any weight. As you know, in the past, compliance has been an issue and I had hoped having gone back to taking his therapy regularly that his viral load would have come down to undetectable levels. However, in September he was still detectable with a viral load of 41,800 and a CD4 count of only 0.0233 x 10^9/l. However, those bloods were taken only a few weeks after going back on regular therapy and, therefore, we are repeating them today. If his viral load is not detectable, I do think that we should now change therapy and I have, therefore, arranged to see him again next month to discuss this further.

Yours sincerely

GRO-C

Dr Margaret Johnson
Consultant Physician in HIV/AIDS

Professor Christine Lee
Consultant Haematologist

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Consultant: Dr Simon A Brown MB MRCP MRCPath
Tele No:0207 830 2068
Fax No :0207 830 2178

Reference: BW/LG/ GRO-B

13 April 2000

Dr GRO-B

GRO-B

Middlesex

GRO-B

Dear Dr GRO-B

Re: GRO-B - DoB: GRO-B 959

GRO-B

Diagnosis: Factor VIII of 5iu/dl.
HIV positive.
Hepatitis-C positive.

I reviewed GRO-B today. He has had no bleeds and has a low level hepatitis-C viral load with a normal liver function test. His major problem is HIV for which he is on combination treatment with Combivir Tbd and Nelfinavir 1250 mg bd. His viral load was 149,000 copies/ml on the 4th of May 1999.

He freely admits to be being poorly compliant with his medication. I have warned him of the risks of ✗ resistance with this approach. He is finding it difficult especially with relationship changes in his life, including separation from his wife.

He is clinically well and only complains of a mild erythematous rash on his forearms and hand. This has been present for the last week. I have taken his bloods today. I have checked his viral load and CD4 count today and suggest that he return if his skin rash does not improve. I have also arranged an appointment for him to see Dr Margaret Johnson.

Septrin commenced.

Yours sincerely,

GRO-C

Dr Barry White MB MRCPI MRCPath
Clinical Research Fellow

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TEL: 0207 830 2068
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Out of hours: 071 794 0500 bleep 811

MAJ/gs/ GRO-B /5th September 2000

GP - Dr GRO-B The Medical Centre
GRO-B
Middlesex GRO-B

Dear Dr GRO-B,

Patient: GRO-B DOB GRO-B 59
GRO-B

Combined HIV/Haemophilia Clinic - 5th September 2000
Consultants: Dr Margaret Johnson - Consultant Physician
Professor Christine Lee - Consultant Haematologist

We reviewed Mr GRO-B in the Combined HIV/Haemophilia Clinic on 5th September 2000. He has not been seen for HIV review for some time but when he last had his blood taken, in April 2000, he continued to have a low CD4 count at 0.036 x 10^9/l and a high viral load with 115,000 copies/ml. He tells me, at that time, he was poorly compliant with therapy. However, for the last few months he tells me his compliance has been very good and he has only missed very occasional tablets. He does find the treatment difficult to take, in particular the Nelfinavir and he also stopped taking his Septrin for the pneumocystis carinii pneumonia prophylaxis as he developed a rash on his arm. However, this was not severe.

We felt, today, that what we needed to do, now he is back on therapy, is see whether this is effective in terms of suppressing his viral load and improving his CD4 count. If the viral load is still detectable then we need to undertake a resistance assay and change his therapy. I have restarted him on high-dose Septrin and told him if he develops a rash to come back to the Haemophilia Clinic for review as we may well be able to treat through and we have, again, reinforced to him how important compliance is in ensuring durability of HIV medication.

Yours sincerely

GRO-C

Dr Margaret A Johnson
Consultant Physician in HIV/AIDS

Professor Christine Lee
Consultant Haematologist

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
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Consultant: Dr Simon A Brown MB MRCP MRCPath

Tele No:
Fax No: GRO-C
E-mail:

CAL/MC GRO-B

24 November 2000

Dr Angela Robinson
Medical Director of the National
Blood Authority
Oak House
Reeds Crescent
Watford
Herts, SD24 4QN

Dear Dr Robinson

I enclosed correspondence from the wife of a patient Mr GRO-B This patient has haemophilia and received a treatment with BPL factor VIII batch number FHE4548 on the 1st November 1997. As you can see from the enclosed letter which was sent at that time there were concerns that the donor pool had been contributed to by a blood donor who subsequently developed new variant CJD. I saw this patient together with his wife on the 31st October and they were particularly concern to know the precise details of the blood donor concern. I explained that this probably was not possible on grounds of confidentiality but I suggested they contacted BPL to find if this was possible.

I would be grateful if you would respond directly about their concerns to Mr and Mrs GRO-B I will copy my letter to you to them so that they know what is happening.

Yours sincerely

Christine Lee
Professor of Haemophilia

CC Mr and Mrs GRO-B

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
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Consultant : Dr. Simon A. Brown MB MRCP MRCPath
Senior Lecturer : Dr. David J. Perry MD PhD FRCP FRCPath
Tel. GRO-C
Fax
E-mail Christine.Lee GRO-C

Dr GRO-B
GRO-B
Edgware GRO-B

Clinic 31st October 2000

Dear Dr GRO-B

Re : Mr. GRO-B, dob GRO-B 59
GRO-B
GRO-B

I saw this patient today together with his wife and Mrs. Miller our social worker. He is 41 years old and has mild haemophilia A with a factor VIII of 5 units per decilitre (normal range 50 – 150). He is infected with both HIV and hepatitis C. He last had treatment for his haemophilia on 12th November when he had an ankle injury playing football.

On functional enquiry he is well although he still has some gastro-intestinal symptoms. He had an endoscopy in October 1999 and the report was normal. He has been two years on medication for his HIV, Combivir - zidovudine 300 mg. bd and 3TC 150 mg. bd together with nelfinavir 1,250 mg. twice a day. Although he has been taking this medication very regularly since seeing Dr. Johnson at the beginning of September and some months before that, earlier in the year his treatment was somewhat erratic. He has re-started his co-trimoxazole 960 mg. x 3 weekly. His last HIV viral load on 6th September was 41,800 which shows a reduction from April 2000 when it was 115,000. He will be reviewed by Dr. Johnson in the next HIV Clinic on 28th November.

He has lost his antibody to hepatitis A and B. He showed a viral load of hepatitis C of 0.6×10^6 in February 1999 although his transaminases have been within normal limits.

We had a long discussion about hepatitis C because both he and his wife are very concerned about this. It is likely he had his first exposure in 1982 and in the past we have shown a PCR which was negative in 1987 and I think that he has previously been given some assurance that he is HCV negative. However, now that we are able to do quantitation we have shown an extremely low viral load in his blood of 0.6×10^6. I have explained to him that I think it is highly likely that he has very little liver damage and that he probably has mounted a good immune response when he became infected with this virus.

His wife was particularly concerned about the risk of infection to herself and their child GRO-B aged six. We did test his wife in June 1998 when she proved to be both HCV and HIV negative.

There was also great concern because he was a patient who received Replenate FHE 4548 on 1st November 1997 and this was one of the batches that was known to have been made from plasma which received a donation from a donor who had new variant CJD. He and his wife requested information about this blood donor and I suggested that they could write to BPL.

He would like to have recombinant factor VIII and I have suggested that he put pressure on his Member of Parliament and the Government. I have provided him and his wife with a copy of a World Federation Monograph about hepatitis C and I intend giving them a photocopy of all the notes so they can come back and discuss the issues further.

Yours sincerely,

Christine Lee
Professor of Haemophilia

Lee, Christine

From: Lee, Christine
Sent: Wednesday, November 15, 2000 1:45 PM
To: GRO-B
Subject: RE: Donor information from BPL

I will write a letter to the director of NBA and copy to you.I think you have collected the notes. Christine Lee

-----Original Message-----
From: GRO-B
Sent: Wednesday, November 15, 2000 12:03 PM
To: Professor CA LEE
Subject: Donor information from BPL

Dear Professor Lee,

I hope that sending a message direct to you by email is not a problem? If you would rather me contact you by post, please let me know.

At GRO-B last review we discussed requesting information from BPL regarding donor information. At that time you said that we could contact them directly, but unfortunately I am having problems in doing this as BPL said they don't have such information and that I should contact Blood Transfusion Centre in Colindale. Colindale inform me that they don't have details of what donor's plasma go into each batch and BPL held this information in the form of ID numbers for each donor, and without this id they could not possible track own individual donor details. I was advised to speak to National Blood Authority HQ in Watford. I managed to speak to them and the Medical Director advises me that information should be requested by Doctor in charge of GRO-B s care, i.e. you. So unfortunately, I am going to have to put the ball in your court and request that if possible could you please deal with this request of GRO-B s behalf.

Thank you for your time and we look forward to hearing from you soon.

GRO-B

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Fax No:
E-mail: Christine.Lee GRO-C

CAL/MC GRO-B

20 November 2000

Dr Angela Robinson
Medical Director of the National
Blood Authority
Oak House
Reeds Crescent
Watford
Herts, SD24 4QN

Dear Dr Robinson

I enclosed correspondence from the wife of a patient Mr GRO-B This patient has haemophilia and received a treatment with BPL factor VIII batch number FHE4548 on the 1st November 1997. As you can see from the enclosed letter which was sent at that time there were concerns that the donor pool had been contributed to by a blood donor who subsequently developed new variant CJD. I saw this patient together with his wife on the 31st October and they were particularly concern to know the precise details of the blood donor concern. I explained that this probably was not possible on grounds of confidentiality but I suggested they contacted BPL to find if this was possible.

I would be grateful if you would respond directly about their concerns to Mr and Mrs GRO-B I will copy my letter to you to them so that they know what is happening.

Yours sincerely

GRO-C

Christine Lee
Professor of Haemophilia

CC Mr and Mrs GRO-B

5 December, 2000

Professor Christine Lee
Professor of Haemophilia
Royal Free Hospital
Pond Street
London NW3 2QG

Dear Professor Lee

Thank you for your letter of 20 November 2000, enclosing correspondence from the wife of a patient of yours, Mr GRO-B who had received BPL factor VIII batch number FHE4548 on 1 November 1997.

I cannot, of course, give you the precise details of the blood donor concerned on the grounds of confidentiality, which applies to all types of voluntary blood, tissue or organ donors. However, I can confirm that the BPL factor VIII batch number FHE4548 did contain one plasma donation from a donor who subsequently went on to develop vCJD. The factor VIII batch pool size contained 26,303 individual donations. Hence, 1 out of 26,303 plasma donations "failed to meet the current health requirements for CJD."

I must emphasise again that the recall of this batch was a precautionary measure as there is still no evidence to suggest that human vCJD can be transmitted by blood or plasma. Indeed, there is increasing evidence to show that there is minimal risk of transmission by fractionated plasma derivatives (i). because of the huge dilutional factor (1 in 26,000) and (ii). spiking studies have shown that the fractionation processes themselves remove the abnormal prion.

I am happy, if you so wish, to copy this letter to your patient, but perhaps it would be better, given the content, that you see the patient and his wife yourself.

My apologies for the difficulties your patient's wife experienced in obtaining more specific information, however, I hope that the details contained in this letter will now satisfy her request.

Yours sincerely

GRO-C

Dr E Angela E Robinson
Medical Director

National
Blood
Authority
Oak House
Reeds Crescent
Watford
Herts. WD1 1QH

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DF

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Fax No:
E-mail: Christine.Lee GRO-C

CAL/MC GRO-

7th December 2000

Mr and Mrs GRO-B
GRO-B
GRO-B

Dear Mr and Mrs GRO-B

This is a response that I obtained from the National Blood Authority

With kind regards

Yours sincerely

GRO-C

Christine Lee
Professor of Haemophilia

HAEMOPHILIA CENTRE & HAEMOSTASIS UNIT
Director: Professor Christine A Lee MA MD DSc(Med) FRCP FRCPath
Senior Lecturer: Dr David J Perry MD PhD FRCP FRCPath
Consultant: Dr Simon A Brown MB MRCP MRCPath
Associate Specialist: Dr Thynn Thynn Yee MBBS MSc MRCP

Tele No: GRO-C
Fax No:
E-mail: Christine.Le GRO-C

CAL/SR/ GRO-B

27 January 2012

Mr & Mrs GRO-B
GRO-B
GRO-B

Dear Mr and Mrs GRO-B

I thought it would be helpful to summarise our consultation yesterday, the 30th of January, when I saw you together with Dr. Thynn Thynn Yee. You had been provided with a photocopy of the notes and you came to discuss these. The following were the issues we discussed:

1. You had noted that on the 1st of April 1985 there was a note that the HTLV III was positive on the 07.02.'85 and that it was noted that GRO-B had been exposed at the GRO-B, when he had been operated on for the cut of the tendons of his hand on the 30th of November 1982. I agree that it was most likely that that was the date, when he became infected with HIV, and he would also have been infected with HCV at that point. The batch number noted was W92508 Armour and you specifically asked whether this had been recalled and whether it had been tested. I explained at that time that the batches were not recalled, because it was only subsequently that it was discovered that they were implicated in HIV transmission. I had no knowledge of any aliquots of this batch been retained.
2. Secondly we discussed hepatitis C infection, clearly GRO-B was exposed on the 30th of November 1982, when he first had treatment with large pool untreated plasma derived clotting factor VIII. The HCV virus was identified in 1989 and we had the first test available in 1991; GRO-B was first tested in 1993, when he was found to be antibody negative and he has been antibody negative on all occasions tested since. We had the ability to test the virus in the blood in 1997 and on the 02.01.1997 he was found to be PCR negative, however, to subsequent the test from for the virus have recorded a very low level of virus, in June 1998 it was 1 x 10^6 and in February 1999 it was 0.6 x 10^6, the transaminases have been within the normal limit throughout. I explained therefore that clinically there was no evidence of liver disease, and no evidence of hepatitis C virus damaging the liver. However, whether GRO-B could be categorised as having cleared hepatitis C naturally (we know that approximately 10 to 20% of our patients do this). It is difficult to interpret, I agree that I would write to Prof. Griffiths, professor of virology, about this and that I would also arrange an appointment for Prof. Dusheiko in the joint liver clinic.

Continued...

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Fax No:
E-mail: Christine.Lee GRO-B

3. We also discussed new variant CJD and I explained that GRO-B had not had one of the implicated batches, which had been notified to us recently where by a blood donor who had new variant CJD had contributed to a plasma pool, which had been used to prepare factor VIII.
4. We finally discussed GRO-B s HIV infection, at the present time he is on Combivir 1 b.d. and Nelfinavir 1,250 mgs b.d. with Co-trimoxazole 960 mgs x 3 weekly. He was seen on the 9th of January by Dr. Johnson and at that time a CD4 count was recorded as being 23/μl with an HIV viral load of 31,800. She had suggested that if that viral load was detectable then he should have his therapy changed, we have arranged for GRO- to attend the clinic with Dr. Johnson on the 20th of February.

With kind regards

Yours sincerely

Christine Lee
Professor of Haemophilia

Cc Dr. GRO-B Middlesex GRO-B

Prof. G. Dusheiko, Medical Unit, R F H

Prof. P D Griffiths, Virology Department, Ground Floor, R F H

Mr GRO-B
GRO-B
GRO-B
GRO-B

20th September 2004

IMPORTANT INFORMATION

Dear Mr GRO-B

Variant Creutzfeldt-Jakob Disease (vCJD) and Plasma Products

This letter is being sent out to all patients and the parents of children with haemophilia, other bleeding disorders and congenital antithrombin III deficiency. It gives new information about certain plasma products available between 1980 and 2001, the possible risk of vCJD and the need for precautionary health care measures following certain medical procedures and surgical operations.

This information does NOT affect ALL patients.

- **PATIENTS AFFECTED** by this information are those with haemophilia, other bleeding disorders or congenital antithrombin III deficiency who received treatment between 1980 and 2001 with clotting factors or antithrombin manufactured by the UK Bio Products Laboratory (BPL) or the Protein Fractionation Centre (PFC) of the Scottish National Blood Transfusion Service (SNBTS) using plasma pools sourced from the UK. These include concentrates of factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complexes as well as antithrombin.

- **PATIENTS NOT AFFECTED** by this information are those who have only ever received recombinant products, DDAVP (desmopressin), clotting factors or antithrombin made with non-UK sourced plasma, or who have never been treated.

If you have ever received a blood transfusion or immunoglobulin this is treated differently and is not covered in this letter.

We realise this information creates uncertainty and may cause you concern.

It is important for everyone to read the rest of this letter and the enclosed 'Information for Patients' that has been prepared to help you understand this changing situation.

What has happened?

You may be aware of product recalls in 1997, 1999 and 2000 when donors who provided plasma used to make clotting factors or antithrombin were subsequently found to have vCJD. These previous notifications involved products made by the Bio Products Laboratory in England and the Scottish National Blood Transfusion Service. You may have been informed at the time.

We are writing to you now to give you further information about these and about further batches of clotting factors or antithrombin that have been made using plasma from donors who later developed vCJD; what action is being taken; and to offer you the opportunity to discuss this with us. None of these batches are now in use.

Who is looking into this?

The CJD Incidents Panel (the Panel) is an expert committee set up by the UK Chief Medical Officers to advise on incidents of possible transmission of CJD through medical procedures. These include treatment with blood or plasma products. When people are diagnosed with vCJD, any blood donations they have given are traced. The Panel has reviewed in detail all batches of plasma products known to date to have been made using plasma from donors who later developed vCJD. We refer to these below as 'implicated' products and batches.

What is the risk from these implicated products?

The Panel has used scientific evidence and expert opinion, together with information from the plasma product manufacturers, to examine the possible risks to health from having received implicated plasma products. This risk is on top of the general risk from eating beef and beef products that may have been contaminated by the agent causing Bovine Spongiform Encephalopathy (BSE or 'mad-cow disease').

The potential additional risk to health depends on the type of plasma product and how each batch was manufactured.

For most batches of implicated products the potential additional risk is so low as to be considered negligible. For example some batches of factor VIII, where only the albumin (which is used to stabilise factor VIII in the vial) has

been sourced from a donor with vCJD, are extremely low risk. However, batches of factor VIII where the clotting factor (and not the albumin) has been sourced from a donor with vCJD, and other implicated products, which include factor IX and antithrombin, carry a higher risk.

What does this mean?

The potential additional risk of actually developing vCJD from receiving any implicated plasma product, on top of the general risk from eating beef, is unknown, but the chances of it happening are likely to be very low.

Some patients who have received certain implicated products do, however, have a greater chance of passing the agent that causes vCJD to others through surgical operations and some other medical procedures. For public health purposes steps need to be taken to prevent spread this way.

Unfortunately, it is likely that further cases of vCJD will occur in people who previously donated blood. This means that more batches of UK-sourced plasma products may be implicated in the future.

Who is affected?

It is likely that special public health precautions will need to be taken for many patients with bleeding disorders or congenital antithrombin III deficiency, because they will have received clotting factors or antithrombin that either are currently implicated (which include particular batches of factor VIII, factor IX and antithrombin) or that may be implicated at a later date. Therefore, **ALL patients with bleeding disorders or congenital antithrombin III deficiency[1] who have received clotting factors or antithrombin derived from UK-sourced plasma[2] between 1980 and 2001 are considered 'at-risk' of vCJD for public health purposes**.

This time period of 1980 to 2001 has been chosen as the most cautious: it runs from when BSE is thought to have entered the human food chain to the last possible expiry date of any product manufactured in the UK that was sourced from UK donors until 1998. Since 1998, plasma for manufacturing plasma products has been imported from the United States.

[1] congenital and acquired haemophilia (Haemophilia A and Haemophilia B), Von Willebrand Disease, other congenital bleeding disorders and congenital antithrombin III deficiency.
[2] factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complexes, as well as antithrombin.

Am I 'at-risk' of vCJD for public health purposes?

If you have received any UK-sourced plasma derived clotting factors or antithrombin between 1980 and 2001, even if you have not received a currently implicated batch, you are 'at-risk' of vCJD for public health purposes.

If you are not sure whether you [your child] have [has] received UK-sourced plasma derived clotting factors or antithrombin between 1980 and 2001, and therefore whether you [your child] are [is] 'at-risk' of vCJD for public health purposes, please contact your Haemophilia Centre. You can do this using the reply form at the end of this letter.

What special precautions should I take?

If you are 'at-risk' of vCJD for public health purposes:

- you should not donate blood,
- you should not donate organs or tissues,
- you should tell whoever is treating you before you undergo medical, surgical or dental treatment, so that they arrange any special procedures for the instruments used in your care.
- It would be best if you tell your family about this in case you might need emergency surgery in the future.

If you are 'at-risk' of vCJD for public health purposes then a note of this will be made in your hospital medical records and will be recorded on the National Haemophilia Database. We will also tell your GP of your 'at-risk' status who will record this in your GP medical notes.

Does this affect my care?

If you are 'at-risk' of vCJD for public health purposes, your clinical care should not be compromised in any way. Healthcare professionals need to know you are 'at-risk' so that if any surgical instruments are used in your care they can be treated differently.

How does this affect my family?

If you are 'at-risk' of vCJD for public health purposes you do not need to take any special precautions in normal life. There is **NO** evidence that vCJD can be passed on between people by:

- living in the same house,
- sharing utensils,
- kissing,
- sexual contact,
- from mother to baby through childbirth or breastfeeding.

Can I find out if I have been treated with an implicated batch?

We are currently checking our patients' records to determine who was treated with UK-sourced clotting factors or antithrombin between 1980 and 2001, which of them have received implicated batches and the extent of their exposure. We will record this in patients' hospital medical notes.

If you would like to find out whether you [your child] have [has] received any of the implicated batches, or you wish to discuss this further with us, please indicate this on the reply sheet. We expect the process of identifying who has received those batches to take some time, as it may involve hand-searching records from many years ago, and liaising with other Centres. We are sorry for this unavoidable delay. We will arrange an appointment for you once we have the information.

If you do not wish to find out whether you [your child] have [has] received one of the implicated batches, please be aware that this information needs to be recorded in the hospital notes. Despite our best intentions, it is possible that this information may become apparent to you [your child] inadvertently, when, for example, looking at your [your child's] medical records.

Whether or not you have received any of the implicated batches or choose to discuss this with us should **NOT** affect your care, as the same special precautions will be taken for **ALL** patients with bleeding disorders or congenital antithrombin III deficiency who received UK-sourced clotting factors or antithrombin between 1980 and 2001.

How can I decide whether to find out if I have received implicated products?

At present there is no known case of a patient with haemophilia developing vCJD through treatment with blood products. There is no diagnostic blood test for vCJD and there is no treatment or cure for this condition. In addition, the same special precautions will be taken for **ALL** patients who have received UK-sourced plasma derived clotting factors or antithrombin between 1980 and 2001, whether or not they have received an implicated batch.

In the light of the above, you may wish to consider carefully whether or not you wish to know if you have received any of the implicated batches.

How can I find out more?

I enclose an information sheet about vCJD developed by the Health Protection Agency alongside the Scottish Centre for Infection and Environmental Health, clinicians' representatives and patients' groups, which I hope will go some way to answering your first questions.

I do appreciate that this information creates uncertainty that may worry and concern you. Do contact the Haemophilia Centre on +44 (0) 207 830 2068 if you wish to talk about this.

Yours sincerely

GRO-C	GRO-C	GRO-C	GRO-C
Professor CA Lee Director	Dr Simon Brown Consultant Haematologist	Dr Thynn Thynn Yee Associate Specialist	Christine Harrington Nurse Consultant

Enc.

Information for patients
Patient reply form
Prepaid envelope for return of patient reply form.

Variant Creutzfeldt-Jakob Disease and Plasma Products
Patient Reply Sheet

Name of patient/child*:
Date of birth:
National Registration Number (if known):
Telephone:
Address:

1. I would like confirmation of whether I/my child* received UK sourced plasma derived clotting factors or antithrombin between 1980 and 2001. These include: factor VIII, factor IX, factor VII, factor XI, factor XIII and prothrombin complexes as well as antithrombin.

IN PERSON / IN WRITING

2. I would like to know if I/my child* received an implicated batch.

YES/NO/DON'T KNOW

3. I would like to have a specific consultation with [the team] to discuss the implications of this issue. Please contact me to make an appointment.

YES/NO

4. I understand that my/my child's exposure to an implicated batch will be recorded in my/my child's hospital and GP notes, and on the National Haemophilia Database.

Signature _____ Date _____

Print name _____

Health Protection Agency

Scottish Centre for Infection and Environmental Health

NHS National Services Scotland

National Public Health Service for Wales

Health, Social Services and Public Safety

Sláinte, Seirbhísí Sóisíalta agus Sábháilteachta Poiblí

VARIANT CREUTZFELDT-JAKOB DISEASE and PLASMA PRODUCTS

INFORMATION FOR PATIENTS

1. What is variant Creutzfeldt-Jakob disease?

Creutzfeldt-Jakob Disease, or CJD, is one of a group of rare and fatal diseases in humans and animals that affect the structure of the brain.

There are four main types of CJD: of these, sporadic CJD (arising spontaneously) is the most common and accounts for 85% of cases. The other types are familial, iatrogenic (through medical treatment) and variant CJD (vCJD). In animals the best-known TSE is bovine spongiform encephalopathy (BSE or 'mad-cow disease'). Variant CJD is believed to be the human form of BSE.

Many people living in the UK have been exposed to BSE (Bovine Spongiform Encephalopathy or 'mad-cow disease') from eating infected beef and so are at a possible risk of developing vCJD.

2. What's this about?

Late last year the death of a person from vCJD who died some years after receiving a blood transfusion from a donor who themselves died of vCJD, was announced. This was the first case of transfusion-associated vCJD infection and increased concern about the possible infectivity of blood. A second probable case was reported in July 2004.

When a patient is diagnosed with vCJD, the UK Blood Services are informed and checks are made to find out whether the patient ever donated blood. Blood products include blood components, which are derived from a single donation of blood, or pools of up to six donations; and plasma products, which are prepared from the pooled plasma of several thousand blood donations in a process known as 'fractionation'.

To date, nine people are known to have donated blood before they became ill with vCJD, and their donations were used to make plasma products. Thus a number of patients may have been exposed to vCJD infection in the course of their past medical care.

This information sheet about vCJD has been developed with doctors' and patients' groups for patients who have been informed by their doctor that they are considered 'at-risk' We hope it will go some way to answering your first questions.

3. Why am I being contacted?

Patients who have received implicated plasma products may be at an additional risk of vCJD. This risk is 'additional' since it is on top of the general risk for many people in the UK from eating beef in the past.

It is impossible to put an exact figure on the chances of getting vCJD, either from BSE-infected beef and beef products, or the possible additional risk from receiving implicated plasma products. So far there have been no cases of vCJD amongst recipients of plasma products sourced from blood donors who later developed vCJD, and the risk of this happening is likely to be very low.

If you received implicated plasma products there is a small possibility that vCJD could have been passed on to you. If so it might be possible for you to pass vCJD on to others in certain circumstances, in which case you and the people providing your healthcare need to take some special precautions to avoid putting other people at potential risk. This is why it is important that you know, even if this causes you anxiety.

4. What measures are already being taken for vCJD?

A number of measures have minimised the risk of getting vCJD from eating BSE-infected meat and meat products. These include banning the feeding of animal protein to other animals, and removing certain parts of animals from the food we eat.

In the healthcare setting, the abnormal 'prion' protein, the infective agent that causes vCJD, is very hard to destroy. Using surgical instruments only once, or destroying those that have been used on patients diagnosed with vCJD, is one way to guard against passing on vCJD. In recent years much effort has also gone into ensuring that the decontamination of all surgical instruments is to the highest standards. The aim is to remove as much potentially infected material as possible.

5. And in relation to blood?

Because it is uncertain whether vCJD can be transmitted by blood the United Kingdom blood services have taken a number of precautionary measures:

- Withdrawal and recall of any blood components, plasma products or tissues obtained from any individual who later developed vCJD (December 1997),
- Importing plasma from the US to manufacture plasma products (1998),
- Removal of white blood cells (leucodepletion) from all blood components (Autumn 1999),
- Importing fresh frozen plasma from the US for patients born on or after 1st January 1996 (Autumn 2002),
- Not accepting donations from people who have received a blood transfusion since 1980 (April 2004),
- Promoting appropriate use of blood and tissues and alternatives throughout the NHS.

6. And in relation to patients?

In 2000 an expert advisory committee called the CJD Incidents Panel (CJDIP) was set up to advise on the handling of 'incidents' of possible transmission of CJD, including vCJD, in a healthcare setting. The CJDIP assesses the risk to other patients, and advises whether patients should be contacted and informed about their possible exposure.

The CJDIP has agreed that, in general, where patients may have been exposed to a 1% or greater possible risk of infection[1], they may have an additional unknown risk of developing vCJD, on top of the general risk from eating beef in the past, and should be contacted. These patients should be given advice about what they should do to avoid putting other people at risk. This advice includes not donating blood, tissue and organs, and informing healthcare professionals so that extra precautions can be taken if they require invasive medical or dental procedures, for example a surgical operation.

There are a lot of uncertainties in estimating the risk of infection with vCJD and a very cautious approach has been taken. The CJDIP has chosen this 1% threshold for informing patients of their exposure so that special precautions can be taken to limit the possible risk of transmitting vCJD between patients. This is considered the best balance between protecting the public from further spread of vCJD and causing excessive anxiety regarding a risk which is uncertain, but thought to be low.

7. So what's new?

Since the CJDIP was established it has been considering policy towards recipients of blood from donors who later developed vCJD.

When people are diagnosed with vCJD, any blood donations they have given are traced. The CJDIP has estimated the potential additional risk of vCJD from treatment with plasma products sourced from all donors known to have later developed vCJD. This risk depends on the type of plasma product and how each batch was manufactured, as well as the amount a patient may have received.

For certain plasma products (e.g. intramuscular immunoglobulin used for travel vaccinations against hepatitis A, or anti D for Rhesus negative pregnant women) the amount of estimated infectivity in the implicated products is so low that the possibility of reaching the 1% threshold can realistically be ignored. Patients who have received these products do not need to take any special precautions.

For other products (e.g. clotting factors and antithrombin, intravenous immunoglobulin, albumin 4.5%) the infectivity may be higher, depending on how the product was made. Once one of these plasma products has been identified the next step is to try to identify those patients who are likely to have had sufficient product to reach the 1% threshold and who need to take special precautions. These patients are considered to be 'at-risk' of vCJD for public health purposes.

[1] A 1% risk of infection means that there is a 1 in 100 possibility that vCJD can be transmitted.

8. Who is affected?

Patients who are considered 'at-risk' of vCJD for public health purposes will be informed by their doctor. The people who may be affected are in three main groups:

- some patients with bleeding disorders (including congenital and acquired haemophilia (haemophilia A and haemophilia B), Von Willebrand Disease, other congenital bleeding disorders) and congenital antithrombin III deficiency,
- some patients with primary immunodeficiency (PID), and
- some patients with other illnesses who might be considered 'at-risk'. These may include, patients with secondary immunodeficiencies; certain neurological conditions and autoimmune illnesses (such as idiopathic thrombocytopaenic purpura), plasma exchange recipients and patients with severe burns. Patients with certain other conditions requiring critical care (including acquired antithrombin deficiency or patients requiring rapid warfarin reversal) may also be affected.

9. How does this affect me?

If you have been informed that you are 'at-risk' for public health purposes, you are being asked to take the following actions in order to reduce the chance of passing on vCJD to other people:

- **Do not donate blood.**
- **Do not donate organs or tissues.**
- **Tell whoever is treating you before you undergo medical, surgical or dental treatment, so they can then arrange any special procedures for the instruments used in your care.**
- **It would be best if you tell your family about this in case you might need emergency surgery in the future.**

A note of this will be made in your hospital medical records and your GP notes. Your care should not be compromised in any way – it will be just the surgical instruments that will be treated differently. Nor will you need extra medical follow-ups because you are 'at-risk' for public health purposes. However, your doctor will always be willing to see you if you have any worries about your health.

10. So if I'm 'at-risk' for public health purposes - what happens now?

You need do nothing other than follow the advice given above (see Section 9).

Normal social contact and household activities do not spread the infection. Your family and friends are not at risk from you and you do not need to take any special precautions in your normal life.

Variant CJD is not infectious in the usual ways. There is no evidence that it can be passed on between people by sneezing or coughing (like colds and flu), sharing utensils, by skin contact, or through kissing or sexual intercourse.

There is also no evidence that vCJD can be sexually transmitted or transmitted from parent to child. However, as a precautionary measure, men who are 'at-risk' of vCJD for public health purposes should also not donate sperm.

11. Does this mean I'm going to suffer from vCJD?

Having reached the 1% threshold does not mean you will actually develop vCJD. This risk is unknown, but the chances of it happening are very low.

There is no evidence for transmission of vCJD by plasma products. Although the process of estimating risk is based on the best evidence available, there is much uncertainty about many aspects. As a result a cautious approach has been taken and may have over-estimated the potential additional risk of vCJD from receiving the various implicated plasma products. Despite these limitations it is still important to take extra public health precautions to provide the best protection for the population in general.

12. Can I be tested to see if I am infected?

No. Scientists are working very hard to develop a test, but as yet there is no test available that can be used to identify someone who may have been infected. Variant CJD can only be reliably diagnosed by brain biopsy or through examining the body after death.

13. What happens if I develop strange symptoms?

CJD causes dementia and a range of other symptoms, including difficulty with balance and extreme clumsiness. Unlike the other forms of CJD, vCJD often starts with psychiatric symptoms like depression and anxiety.

Go and see your doctor. It is unlikely that 'strange symptoms' will be the start of vCJD but your doctor will be able to arrange for you to see an expert if appropriate.

14. Will this mean I won't be able to get life insurance?

The Association of British Insurers have informed the CJDIP that their members will not refuse insurance just because someone is categorised as 'at-risk' for public health purposes.

15. General information about vCJD

What is the cause of vCJD?

Infections like influenza and pneumonia are caused either by viruses or bacteria. Some stomach infections are caused by microscopic parasites. Variant CJD, and the other TSEs, are different from these common infections. The cause is an abnormal infectious protein known as a 'prion'.

There is no test, treatment or cure for vCJD at present and the disease is always fatal. Scientists are researching the causes and possible tests and treatments for the disease.

How do you catch vCJD?

Variant CJD is believed to be caused in the first instance by exposure to the abnormal prion protein that causes BSE. Many of the UK population have been exposed through eating BSE-infected beef and beef products in the 1980s and early 1990s.

Variant CJD may also be transmitted between patients in the healthcare setting. So far there are no recorded instances of vCJD being spread through surgery, nor have there been any cases amongst recipients of plasma products sourced from individuals who later developed vCJD.

How many cases of vCJD are there?

So far, almost 150 cases of vCJD have occurred in the UK and a handful in other, mainly European, countries.

It is thought that the UK epidemic may have reached a peak. However no one knows how many people will contract this disease in the future.

16. Sources for Additional information

The process of informing patients about their possible additional risk status, and the special precautions they may need to take is being coordinated by the Health Protection Agency (HPA) in England, Wales and Northern Ireland, and in Scotland by the Scottish Centre for Infection and Environmental Health (SCIEH).

More information about vCJD with useful links is available from their websites
HPA: http://www.hpa.org.uk/infections/topics_az/cjd/menu.htm
SCIEH: http://www.show.scot.nhs.uk/scieh

Further information is also available from:

The Haemophilia Society http://www.haemophilia.org.uk
The Primary Immunodeficiency Association http://www.pia.org.uk
CJD Support Network http://www.cjdsupport.net
Human BSE Foundation http://www.hbsef.org
National CJD Surveillance Unit http://www.cjd.ed.ac.uk
Department of Health http://www.doh.gov.uk/cjd/index.htm
National Prion Clinic
http://www.st-marys.org.uk/specialist/prion/index_prion.htm
National Public Health Service for Wales
http://www.wales.nhs.uk/sites/home.cfm?OrgID=368
NHS Direct Online http://www.nhsdirect.nhs.uk

NHS Direct and its national colleagues are also operating a 'vCJD and Plasma Products' advice line for general enquiries (telephone: 0845 850 9850).

VARIANT CREUTZFELDT-JAKOB DISEASE (vCJD) and PLASMA PRODUCTS

CLINICAL INFORMATION

Health Protection Agency

Scottish Centre for Infection and Environmental Health

NHS National Services Scotland

Health, Social Services and Public Safety

1. Introduction

In 2000 an independent expert advisory committee, the CJD Incidents Panel (CJDIP), was established on behalf of the UK Chief Medical Officers to advise all those bodies responsible for the provision and delivery of health care on how to manage incidents involving the potential transmission of CJD between patients.

The CJD Section of the Health Protection Agency (HPA), based at Colindale, North-West London, provides the secretariat to the CJD Incidents Panel. It is coordinating the notification of patients who may have been exposed to variant CJD (vCJD) through implicated plasma products, in liaison with clinician and patient groups in the UK. The HPA is handling this notification in England, Wales and Northern Ireland. The Scottish Centre for Infection and Environmental Health (SCIEH) is handling this notification in Scotland.

This booklet is aimed at clinicians and other staff at local level who may be involved in notifying those patients who have received vCJD-implicated plasma products. This may also be used to supplement the accompanying Patient Information Sheet.

2. Background

In 1997, 1999 and 2000 the UK national blood services were advised of donors who later developed vCJD. The implicated products that had been manufactured from plasma donated by these donors were identified and consignees were notified according to guidance at the time. These earlier notifications did not involve placing patients in a group 'at-risk' for vCJD. However some recipients were traced and informed by their clinician.

The situation has changed. Regarding plasma products, the CJD Incidents Panel currently advises that certain special public health precautions need to be taken for some recipients of UK sourced plasma products who may have been exposed to potential vCJD infectivity. This is in order to reduce any possible risk of onward transmission of vCJD. These new recommendations were not available at the time of previous notifications. In December 2003 a case of transfusion-associated vCJD was announced, increasing concern regarding the potential vCJD infectivity of blood. A second probable case of transfusion-associated vCJD infection was reported in July 2004.

To date, nine UK plasma donors are now known to have developed vCJD. Collectively, they have made 23 plasma donations. The donated plasma has been used to manufacture factor VIII, factor IX, antithrombin, intravenous immunoglobulin G, albumin, intramuscular human normal immunoglobulin and anti-D.

3. Public health precautions against vCJD

Several public health measures have been implemented to minimise the risk of transmission of vCJD to humans from meat and meat products infected with Bovine Spongiform Encephalopathy (BSE or 'mad-cow disease'). These include banning the feeding of mammalian protein to other mammals, and removing certain high-risk tissues from the human food chain.

Other public health measures are aimed at minimising any possible risk of transmitting vCJD between people. These include:

- Measures to protect the blood supply,
- Improving decontamination standards for surgical instruments, and
- Taking special infection control precautions when operating on patients with, or 'at-risk' of, vCJD.

Special precautions are needed because standard decontamination processes cannot be relied on to remove all the infectivity from instruments used on patients with vCJD.

When someone is considered to be 'at-risk' of vCJD for public health purposes, they are asked to take certain special precautions to reduce the risk of spreading the infection to others. These include:

- Not donating blood, tissue and organs, and
- Informing their medical carers so that extra infection control precautions can be taken should they require future medical care. This subject is considered in more detail in Section 9.

4. Public health precautions in relation to blood

The risk of transmitting vCJD through blood remains uncertain. The Department of Health (England) commissioned an assessment of this risk by Det Norske Veritas (DNV) Consulting, which was assessed by the Spongiform Encephalopathy Advisory Committee (SEAC) and accepted in early 1999.

As a result several public health precautions have been taken to reduce any possible risk of transmitting vCJD through blood. These precautionary measures include:

- Withdrawal and recall of any blood components, plasma products or tissues obtained from any individual who later develops vCJD (December 1997).
- Importing plasma from the USA for fractionation to manufacture plasma products (1998).

- Removal of white blood cells (which may carry the greatest risk of transmitting vCJD) from all blood used for transfusion (leucodepletion) (October 1999).
- Importing fresh frozen plasma from the United States for patients born on or after 1st January 1996 (August 2002).
- Not accepting donations from people who have themselves received a blood transfusion in the UK since 1980 (April 2004). This has been extended to include two new groups: apheresis donors and donors who are unsure if they had previously had a blood transfusion (August 2004).
- Promotion of appropriate use of blood and tissues and alternatives throughout the NHS.

5. CJD related healthcare incidents

CJD incidents occur when there is a possibility that patients could have been exposed to CJD, or vCJD, either through exposure to contaminated instruments, through transplantation, blood transfusion or treatment with plasma products. This includes situations in which people have received blood transfusions or plasma products derived from donors who have subsequently developed vCJD.

The CJDIP advises on the handling of these incidents, which includes advice on the management of patients who could have been exposed to vCJD. Local infection control teams and health protection teams should seek advice from the CJDIP on how to manage these incidents. The CJDIP assesses the risk to these patients, and advises whether patients should be contacted and informed about their possible exposure. These patients are then advised whether special public health precautions need to be taken to prevent possible transmission to other patients.

More information on the CJDIP is available on the HPA website at: http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm. This includes the CJDIP Framework document, which sets out the principles of managing CJD incidents and also describes the risk assessment models that underpin the risk management of surgical and blood incidents.

6. Calculation of potential vCJD infectivity in plasma products

The CJDIP has considered the risk to people who have received originating from donors who subsequently developed vCJD. Det Norske Veritas Consulting have carried out a risk assessment to inform the management of these incidents. This uses published experimental data to model the potential vCJD infectivity in blood, its various components, and in plasma products. In Autumn 2003 this risk assessment was accepted by SEAC, the Committee on the Microbiological Safety of Blood and Tissue, and the Committee on Safety of Medicines. This DNV risk assessment is available at:

[http://www.dnv.com/consulting/news_consulting/RiskofInfectionfromvariantCJDinBlood.asp].

The CJDIP has used the Risk Assessment together with information on how batches of plasma products are manufactured, to assess the potential levels of infectivity in different plasma products that would be used to treat patients, as follows:

- Plasma that had been donated by people who subsequently developed vCJD was traced through the National CJD Surveillance Unit, Edinburgh and national blood services to identify the specific batches of plasma products made from these patients' blood.
- Plasma product manufacturers supplied the relevant data on each implicated batch, so that the infectivity in each could be estimated.
- The CJDIP then applied the infectivity estimates in the DNV report to the detailed circumstances involved in the manufacture of these batches. (For each of the major assumptions underlying the risk assessment, the most precautionary option was chosen.)

The final calculations indicate the potential level of vCJD infectivity in different plasma products that were used to treat to patients

7. Recommendations of the CJD Incidents Panel

The potential risk of vCJD infection following treatment with any implicated plasma derivative, on top of the risk from dietary exposure to the bovine Spongiform Encephalopathy (BSE) agent, is very uncertain. However, some patients treated could pose a potential risk to others in certain circumstances.

The CJD Incidents Panel advises that patients who have been exposed to an estimated 1% or greater potential additional risk of vCJD infection, whether from contaminated instruments, through transplantation, or by blood transfusion or treatment with implicated plasma products, should be contacted and advised that they are 'at-risk' of vCJD for public health purposes and should take special public health precautions.

The likelihood of patients being 'at-risk' of vCJD for public health purposes following exposure to implicated plasma products, should be categorised as follows:

- **High:** the amount of potential vCJD infectivity in product batches is high enough for patients to be considered 'at-risk' of vCJD for public health purposes following the administration of a very small dose (e.g. one treatment with Factor VIII, Factor IX or antithrombin where one vial used has been implicated).

- **Medium:** the amount of potential vCJD infectivity in product batches is not low enough to be ignored but substantial quantities of the material in question would need to be administered for patients to be considered 'at-risk' of vCJD for public health purposes (e.g. several infusions of intravenous immunoglobulin, or large doses of albumin 4.5%).

- **Low:** the amount of potential vCJD infectivity in product batches is so low that the likelihood of a patient being considered at potential additional risk of vCJD infection can realistically be ignored (e.g. albumin 20%, factor VIII products where the albumin excipient (which is used in the manufacturing process to stabilise the factor VIII concentrate in the vial) and not the plasma concentrate itself, has been implicated, intramuscular human normal immunoglobulin (used, for example, for travel prophylaxis against hepatitis A), and anti-D.)

The uncertainties underlying the assessment of risk are great, and several precautionary assumptions are involved. **The 'at-risk' threshold is a guide for implementing special public health precautions to limit any possible human-to-human transmission of vCJD. It should NOT be used as a precise guide for advising individuals about their potential additional risk of developing vCJD.**

8. Identifying recipients of implicated plasma products

8.1 Patients with bleeding disorders[1]:

Treatment with UK-sourced factor VIII (where the plasma concentrate used in the manufacturing process has been implicated), factor IX or antithrombin is highly likely to expose patients to this potential additional risk. This is because a single dose of these products, as used in clinical practice, is estimated to contain sufficient potential vCJD infectivity to cross the 1% threshold. Treatment with factor VIII where only the albumin excipient used in the manufacturing process, and not the plasma concentrate, has been implicated, is very unlikely to expose patients to a 1% or greater potential additional risk. This is because several thousand vials of the implicated product would be needed, and this is not likely to occur in clinical practice.

It is likely that many patients with bleeding disorders will have been exposed to a potential additional risk of 1% or greater. It is also likely that further batches of UK-sourced plasma products will be implicated in the future as more cases of vCJD arise. For these reasons UK Haemophilia Doctors and

[1] defined here as congenital and acquired haemophilia (Haemophilia A and Haemophilia B), Von Willebrand Disease, other congenital bleeding disorders **and** congenital antithrombin III deficiency.

patient representatives believe the Panel Recommendations should be that **all patients with bleeding disorders[1] who have been treated with UK-sourced pooled factor concentrates** or **antithrombin[2] between 1980 and 2001[3] should be considered 'at-risk' of vCJD for public health purposes and special precautions taken.** The CJDIP and UK Health Departments have endorsed this approach.

If there is uncertainty about whether a patient has received UK-sourced pooled factor concentrate or antithrombin between 1980 and 2001 (eg due to incomplete records), then the patient should **NOT** be considered at risk of vCJD for public health purposes.

Patients who have died within the last year should also be assessed, and if identified as 'at risk', have their clinical history reviewed in order to identify and manage any recent surgical incident that may pose an infection control risk (see section 9). When centres identify 'at-risk' patients who are currently treated elsewhere, the centre doctor should contact the clinician currently responsible for the patient's care, so they may manage the patient appropriately.

All patients with bleeding disorders are to be informed about the situation. The clinical care of the patients identified as 'at-risk' for public health purposes should not be compromised in any way.

All patients with bleeding disorders who are 'at-risk' of vCJD for public health purposes are to be given the option of finding out whether or not they received known implicated batches. This includes batches that are highly likely to expose patients to a 1% or greater potential additional risk (factor VIII where the plasma concentrate has been implicated, factor IX and antithrombin) as well as batches for which this likelihood is so low as to be considered negligible (factor VIII where the albumin excipient has been implicated). Patients should also be made aware that with future recognition of implicated batches, any assessment of their individual exposure might change. Whatever their choice this information will not affect their management as **ALL** patients who have received UK-sourced pooled factor concentrates and antithrombin as described above will be managed in the same way, i.e. as 'at-risk' of vCJD for public health purposes (see Section 9).

Patients 'at-risk' of vCJD for public health purposes should be informed that their 'at-risk' status will be recorded in their hospital medical records and primary care notes. The extent of exposure to implicated batches, and whether or not a patient has asked to know if they have received implicated

[2] ie. clotting factors and antithrombin made from pooled plasma. These include factor VIII, factor IX, factor VII, factor XI, factor XIII, and prothrombin complex concentrates as well as antithrombin.

[3] The start date of 1980 is when BSE is thought to have entered the human food chain. The end date of 2001 is the last possible expiry date of any product manufactured by the UK fractionators that was sourced from UK donors until 1998.

batches, will also be recorded on a Patient vCJD Exposure Assessment Form to be placed in their hospital medical records. This assessment is important for public health monitoring and to inform public health precautions and future policy for this patient group. If further batches of plasma products are found to have been sourced from donors who have developed vCJD (as a result of trace-back from new vCJD cases), the exposure record of 'at-risk' patients will need to be updated.

Haemophilia centres should use the Patient vCJD Exposure Assessment Form in response to the UKHCDO/Department of Health vCJD Surveillance study, which collects data on patients with bleeding disorders who have been exposed to implicated plasma products, and monitors their outcomes. The form is anonymous; a copy should be sent in confidence to the UKHCDO National Haemophilia Database Coordinator. The information will also be used when public health policy for this patient group is reviewed.

8.2 Primary Immunodeficiency (PID) Patients:

Eleven batches of Vigam (intravenous immunoglobulin G) released by BPL, are known to have been manufactured from donations from people who later developed vCJD. Nine of these batches may have been used to treat patients with primary immunodeficiency between December 1996 (the first release date) and February 2000 (the last expiry date)[4]. Substantial doses would need to be administered before a patient is classified as 'at-risk' of vCJD for public health purposes, and special precautions taken (Section 9).

Intravenous immunoglobulins manufactured by other manufacturers, in particular, the Protein Fractionation Centre (PFC) of the Scottish National Blood Transfusion Centre, have **NOT** been implicated to date.

The CJDIP advises that all patients with primary immunodeficiency who have received implicated batches of Vigam manufactured by BPL and **who have been assessed as having been exposed to a 1% or greater potential additional risk of infection** should be considered 'at-risk' of vCJD for public health purposes. Patients who have not received implicated batches, or who have received an insufficient dose of an implicated batch to be considered at a potential additional risk of 1% or greater, are **NOT** affected.

All patients with PID are being informed of the situation. Because most of these patients will not have had sufficient exposure to be classified as 'at-risk' of vCJD for public health purposes, an individual risk assessment will be carried out on **ALL** who received Vigam between December 1996 and February 2000 and who therefore may have been exposed. This risk assessment can be completed locally using a Patient vCJD Exposure Assessment Form provided by the HPA for PID patients.

[4] The remaining two batches were used as part of a clinical trial for ITP (trial coordinators are being contacted directly and these batches followed up separately)

The Patient vCJD Exposure Assessment Form will record the patient's known exposure to the implicated products; include an uncomplicated method for calculating whether the 'at-risk' threshold has been reached; and provide a record of the patient's current 'at-risk' status to be placed in their hospital medical records. It will also record whether or not a patient has asked to know if they have received implicated batches (see below). All patients should be informed of this fact. If further batches of plasma products are found to have been sourced from donors who have developed vCJD (as a result of trace-back from new vCJD cases), the exposure record and risk assessment of all patients will need to be updated.

Collation of individual assessments is important for public health monitoring and to inform public health precautions and future policy for this patient group. For this reason for each patient who is assessed to be 'at-risk' of vCJD for public health purposes a copy of the Patient vCJD Exposure Assessment Form should be sent in confidence to the Consultant Head of the CJD Section at the HPA-Communicable Disease Surveillance Centre in Colindale (via SCIEH in Scotland), where all clinical data is managed in accordance with Caldicott guidance, the requirements of the Data Protection (1998), and the Health and Social Care (section 60, 2001) Acts.

Patients' individual risk assessments should be based on the implicated batches of immunoglobulin that a patient is known to have received. Where there is doubt, e.g. because of gaps in a patient's treatment record, then the patient should **NOT** be included in the 'at-risk' group.

Patients who have died within the last year should also be assessed and, if identified as 'at-risk', have their clinical history reviewed in order to identify and manage any recent surgical incident that may pose an infection control risk (see section 9). When centres identify 'at-risk' patients who are currently treated elsewhere, the centre doctor should contact the clinician currently responsible for the patient's care, so they may manage the patient appropriately.

Those patients who received Vigam between December 1996 and February 2000 who are assessed to be 'at-risk' of vCJD for public health purposes will be informed after consultation with their current GP. They should be informed that their 'at-risk' status will be recorded in their hospital medical records and primary care notes. The clinical care of the patients identified as 'at-risk' for public health purposes should not be compromised in any way.

Patients who did not receive Vigam between December 1996 and February 2000, or who did but are assessed to be not 'at-risk' of vCJD for public health purposes, will also be contacted. Patients who received Vigam between December 1996 and February 2000 should be informed that the extent of their exposure will be recorded in their hospital medical records. These patients should be advised they are not currently considered 'at-risk' of vCJD

for public health purposes, although the extent of their exposure might change if other product batches are implicated in the future. They should also be given the option of finding out if they received any of the implicated batches of Vigam, even though this would be insufficient to place them 'at-risk' of vCJD for public health purposes.

8.3 Other patients who may be at potential additional risk:

In addition to patients with bleeding disorders and primary immunodeficiency there are a variety of other patients whose treatment may have involved sufficient quantities of implicated plasma products for them to be considered 'at-risk' of vCJD for public health purposes.

It is not possible to give an exhaustive list but examples include:

- conditions requiring several infusions of intravenous immunoglobulin G (including secondary immunodeficiencies; certain neurological conditions and autoimmune illnesses such as idiopathic thrombocytopaenic purpura),
- conditions requiring large volumes of albumin 4.5% (including plasma exchange recipients and patients with severe burns)
- patients with certain other conditions requiring critical care (including acquired antithrombin deficiency or patients requiring rapid warfarin reversal).

Blood Transfusion Laboratories, Hospital Blood Banks and Hospital Pharmacies are being asked via their Medical Directors to assess the traceability of the implicated batches back to particular patients.

The CJDIP advises that patient notification should be considered only where records are readily accessible and patients can be easily identified as having received implicated batches. Only in such circumstances is the trace-back effort likely to be proportionate to any possible public health benefit.

If patients are identified as having received implicated batches, the responsible clinician is asked to forward a copy of the Patient vCJD Exposure Assessment Form in confidence to the Consultant Head of the CJD Section, at the HPA-Communicable Disease Surveillance Centre in Colindale (via SCIEH in Scotland), who will undertake an individual risk assessment to decide whether the patient should be considered 'at-risk' of vCJD for public health purposes. The clinical data forwarded will be managed in accordance with Caldicott guidance, the requirements of the Data Protection (1998), and the Health and Social Care (section 60, 2001) Acts.

Patients' individual risk assessments should be based on the batches of implicated product that a patient is known to have received. Where there is

doubt, e.g. because of gaps in a patient's treatment record, then the patient should **NOT** be included in the 'at-risk' group.

Patients who have died within the last year should also be assessed and if identified as 'at-risk' have their clinical history reviewed in order to identify and manage any recent surgical incident that may pose an infection control risk (see section 9). Patients whose care has been transferred elsewhere should be followed up if they are assessed to be 'at-risk' of vCJD for public health purposes.

9. Public health precautions for 'at-risk' patients

9.1 Advice to patients and their general practitioners

Patients considered 'at-risk' of vCJD for public health purposes[5] are asked to take certain special public health precautions: not to donate blood, organs or tissues and to inform their clinician if they need medical, surgical or dental treatment, so that extra infection control precautions can be taken to reduce any possible risk of spreading vCJD.

All patients who are considered 'at-risk' of vCJD for public health purposes should be advised to inform clinicians of this fact so that extra infection control precautions can be taken should they require future medical care. They should be asked to inform all healthcare professionals, for example, in private clinics, not just those working in the NHS. Patients should also be asked to inform their families, in case the patient needs emergency surgery in the future.

Patients who are considered 'at-risk' of vCJD for public health purposes should also have their 'at-risk' status recorded in their hospital medical records and primary care notes.

The clinician responsible for a patient who is 'at-risk' of vCJD for public health purposes should contact their patient's general practitioner so they may:

- know that their patient is being informed about their 'at-risk' status,
- record the patient's vCJD 'at-risk' status and the special precautions required in their primary care records,

[5] These include patients who are considered 'at-risk' of vCJD for public health purposes because of their exposure to implicated plasma products, as well as patients treated with implicated single unit blood components, such as fresh frozen plasma, cryoprecipitate, red blood cells or platelets, donated by people who subsequently developed vCJD. For recipients of single unit blood components these steps are already in place. Patients treated with vCJD implicated single unit blood components are identified by the UK national blood services and the National CJD Surveillance Unit, Edinburgh. Local health teams are then advised to contact these patients so they can take public health precautions.

- include this information in any referral letters should the patient require invasive medical or dental procedures, for example a surgical operation (guidance on infection control for any patient who is considered 'at-risk' of vCJD was published by the ACDP TSE Working Group in 2003 [http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm],
- check if the patient has undergone any surgery within the past 12 months at other hospitals, and if they have, liaise with their local Health Protection Team in order to ascertain whether any further action needs to be taken.

The clinical care of the patients identified as 'at-risk' for public health purposes should not be compromised in any way.

9.2 Future donation of blood, tissue and organs:

Patients who are considered 'at-risk' of vCJD for public health purposes are advised not to donate organs, tissues or blood. Many patients who have received implicated plasma products and who may be at a potential additional risk of 1% or more, e.g. those with bleeding disorders or primary immunodeficiency disease, are already excluded from donation because of their underlying condition.

There is no evidence that vCJD can be sexually transmitted or transmitted from parent to child. However, as a precautionary measure, men who are 'at-risk' of vCJD for public health purposes should be advised not to be sperm donors.

9.3 Future surgery and invasive medical procedures:

Revised guidance on infection control for any patient who is considered 'at-risk' of vCJD was published by the ACDP TSE Working Group in 2003: http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm. This document describes the infection control measures that should be taken in hospital care, in surgery, and community healthcare including dentistry. A new 'endoscope' annex to this guidance is to be published imminently. This TSE Infection Control Guidance should be followed.

When patients who are 'at-risk' of vCJD for public health purposes need to undergo an invasive medical procedure, they should inform the doctor or nurse in charge of their care about this so that special infection control precautions can be taken.

This information might also be included in the referral letter. Patients should also be asked to inform their families, in case the patient needs emergency surgery in the future.

9.4 Dentistry:

Patients considered 'at-risk' of vCJD for public health purposes should inform their dentist about this. This will enable the dentist to ensure satisfactory standards of infection control are used. Dentists may also include the information in referrals to specialists such as maxillofacial surgeons.

The TSE Infection Control Guidance states that:
"The risks of transmission of infection from dental instruments are thought to be very low provided optimal standards of infection control and decontamination are maintained. General advice on the decontamination of dental instruments can be found in guidance prepared by the British Dental Association (BDA) on 'Infection control in dentistry'. This document (known as the 'A12') is available from the BDA and can be accessed on their website at www.bda-dentistry.org.uk. Dental instruments used on patients defined in Table 4a [this includes patients 'at-risk' in relation to vCJD] can be handled in the same way as those used in any other low risk surgery i.e. these instruments can be reprocessed according to best practice and returned to use. Optimal reprocessing standards must be observed. Additionally, dentists are reminded that any instruments labelled by manufacturers as 'single use' should not be re-used under any circumstances.

"There is no reason why any of the categories of patients defined in Table 4a [as 'at-risk' for public health purposes] or their relatives should be refused routine dental treatment. They can be treated in the same way as any member of the general public."

9.5 Previous surgery, invasive medical procedures and donations:

Many patients considered 'at-risk' of vCJD for public health purposes may have undergone surgery in the time that has elapsed since their possible exposure to vCJD. If this is the case, surgical instruments that have come into contact with medium or high risk tissues[6] could pose an infection risk to other patients. This is because the infective agent for vCJD, the abnormal 'prion' protein (PrP^{Sc}) is not completely removed by routine decontamination processes.

Any risk of transmitting vCJD on such surgical instruments will decrease each time they are used and decontaminated. After going through approximately ten cycles of use and standard decontamination, the instruments are unlikely to pose a significant risk of infection to other patients.

[6] High risk tissues in vCJD are currently defined as the central nervous system and posterior eye. Medium risk tissues in vCJD are currently defined as: the olfactory epithelium, anterior eye and cornea, gastrointestinal lymphoid tissue (including tonsil, appendix and rectum) and peripheral lymphoid tissue. Tissues of concern include the spleen, lymph nodes, thymus and adrenal gland. (see the ACDP TSE Working Group guidance http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/Index.htm (section 4.41)

Recent procedures on medium or high risk tissues in which instruments may not have undergone ten cycles of use and standard decontamination since being used on an 'at-risk' patient should be reported promptly to the CJDIP by the local hospital infection control team as described at :
http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm.The incident should be reported using the reporting form available on this website.

Surgical units vary in how often different instruments are re-used and decontaminated. A review of each 'at-risk' patient's surgical history over the previous 12 months should reveal any instruments that still pose a potential risk to other patients.

The surgical records of patients 'at-risk' of vCJD who have died within the last year should be reviewed in the same way.

The CJDIP may advise that instruments used in these procedures should be quarantined immediately or destroyed. The CJDIP currently advises that patients exposed to these instruments in subsequent operations do not need to be contacted. This advice would be reviewed should an 'at-risk' patient develop vCJD.

Provided that standard decontamination processes have been used, other operations that have been undertaken on these 'at-risk' patients do not need to be investigated further or reported to the CJDIP.

Donations of blood, tissues or organs made by 'at-risk' patients since they were possibly exposed to vCJD, should be reported to the CJDIP. The CJDIP advises that patients who have received blood, tissues or organs donated by any of these 'at-risk' patients do not need to be contacted. This advice will be reviewed as new scientific evidence emerges in this field.

10. Advice and care for 'at-risk' patients

The information that has to be given to patients who may be 'at-risk' of vCJD for public health purposes through exposure to implicated plasma products may be devastating.

It is quite likely that your patient will want you to give them an absolute guarantee that they will not develop vCJD. This is clearly not possible, as many in the UK will have had possible dietary exposure to the BSE agent responsible for vCJD, and the potential additional risk of actually developing vCJD from receiving any implicated plasma product, on top of the general risk from eating beef, is unknown. However the chances of it happening are likely to be very low. Everyone also has a very small but measurable risk of developing sporadic CJD (see Section 11).

Providing this information will require careful consideration and preparation, including making arrangements for follow up discussions with appropriate health care staff.

Infectivity:

Routine contact with people who have CJD, including vCJD and those considered 'at-risk' of vCJD, does not pose a risk for relatives, healthcare workers or the community at large. CJD is not infectious in the usual way - by airborne droplets (like colds and flu) or by skin contact or through sexual intercourse. There is no evidence that vCJD could pass between people from mother to child.

Treatment for vCJD:

There is no test, treatment or cure for vCJD at present, nor is there likely to be in the foreseeable future although research is underway into the causes, tests and potential treatments for the disease.

Discussion of implications:

Decisions will need to be made locally regarding how patients will be informed about their potential additional risk of developing vCJD. Many patients are likely to require more than one session to discuss the implications of the news if they are to come to terms with the impact of what they have been told. Advice on managing this process may be sought from a trained counsellor.

11. About CJD

11.1 General

Creutzfeldt-Jakob Disease (CJD) is one of a rare group of diseases, known collectively as 'transmissible spongiform encephalopathies' (TSEs), which affect the structure of the brain causing dementia and a range of neurological symptoms, including ataxia and jerky movements.

A number of TSEs are recognised in both humans and animals. In animals, the best-known TSE is bovine spongiform encephalopathy (BSE or 'mad-cow' disease'). In humans, there are four main types of CJD: of these, sporadic CJD accounts for 85% of cases. The other types are familial, iatrogenic and vCJD.

At present, TSEs, including CJD, can only be reliably diagnosed by the histological examination of central nervous system tissue following a brain

biopsy or after a post mortem. There is no test for CJD, no treatment and the disease is universally fatal.

11.2 Types of CJD

Sporadic CJD

Sporadic CJD is most common in the over 50s, and affects about one person per million per year worldwide. It is thought to arise spontaneously. Early symptoms are usually of mental deterioration or behavioural disturbance. A rapidly progressive dementia with obvious multifocal neurological involvement soon develops and within weeks the patient may become unsteady on their feet, lacking in co-ordination and markedly clumsy. In some people these are the first symptoms. Later symptoms may include blurred vision or even blindness, rigidity in the limbs, sudden jerky movements, and incontinence. The course of the disease is typically measured in months.

Familial CJD

Familial CJD has an autosomal dominant inheritance. The patients are often younger and the duration of the illness has a longer time course than sporadic CJD. Between six and ten cases are seen each year in the UK. The clinical features of genetic CJD are variable, even within affected families. Some patients exhibit clinical features that resemble sporadic CJD, while others present with ataxia and other movement disorders before the onset of dementia.

Iatrogenic CJD

Iatrogenic CJD occurs through inoculation with infected tissue either via surgical procedures or transplant of infective material, or through treatment with human pituitary derived hormones such as human growth hormone. The clinical features of this diverse group of patients are partially dependent on the route of transmission. Worldwide there have been four cases associated with neurosurgery with a mean incubation period of about 18 months. Two cases have been linked to the use of depth electrodes used on the brain and a further two to corneal transplants. About 150 people have been infected following grafting with contaminated dura mater, and over 100 people through treatment with contaminated human growth hormone. There have been two cases of probable transmission of vCJD infection associated with blood transfusion in the UK (announced late 2003 and 2004) to date.

Variant CJD (vCJD)

Variant CJD was first recognised in 1996 and is thought to be caused, in the first instance, by dietary exposure to the BSE agent of cattle, although no-one knows the exact route of infection. It typically affects younger people with a median onset age in the late 20s, and symptoms differ from those of sporadic

CJD in that they are often psychiatric at onset, such as anxiety and depression, and there may be persistent pain, with odd sensations in the face and limbs. These are followed by more obvious neurological symptoms and progressive dementia. Variant CJD also differs from other human TSEs in that the transmissible agent is detected outside the nervous system, as well as inside, especially in the lymphoid tissues throughout the body. Variant CJD has a relatively longer time course than most other forms of CJD, with an average period of 14 months between the onset of symptoms and death.

Almost 150 cases of vCJD have occurred in the UK and a small number in other countries. It is thought that the UK epidemic may have reached a peak and the latest estimates have been revised downwards from some of the pessimistic forecasts that were made in the mid-1990s. However no-one knows how many people will be diagnosed with this disease in the future. Further information, including monthly numbers of cases and the latest short-term incidence projection is available from the National CJD Surveillance Unit's website: http://www.cjd.ed.ac.uk.

11.3 Abnormal prion protein (PrPSc)

The cause of CJD is thought to be an abnormal form of the naturally occurring prion protein (PrP) that can be infectious. In its normal form, designated as PrP^{C}, this protein occurs in the brain and other parts of the body in humans and a wide range of animals; its function is unknown. The abnormal prion protein, designated as PrP^{Sc}, is chemically identical to the normal form but its physical shape is different, making it resistant to normal cell degradation. It is thought to build up by inducing normal protein to misfold, although how this change occurs is unknown. These changes lead to accumulation in various tissues, with the highest levels occurring in the central nervous system where tissue damage is most severe. As the disease progresses there is loss of neuronal tissue which gives rise to the characteristic 'spongiform' appearance of the brain.

One important effect is that there is no discernible response from the immune system. In addition, the abnormal prion protein is resistant to most of the common methods used for inactivating bacteria and viruses. As a consequence, prions are not totally inactivated by heat, ultraviolet light or other standard sterilisation procedures such as immersion in sodium hypochlorite at normal concentrations. Autoclaving cannot be relied upon to denature any abnormal prion protein remaining on surgical instruments following surgery.

The initial abnormal prion protein needed to seed the above process may occur spontaneously as a rare event (a possible explanation for sporadic CJD); be associated with an inherited genetic abnormality of the PrP gene (familial CJD); or be acquired, either from contamination with tissue from an infected person in a medical setting (iatrogenic CJD) or, as in vCJD, most likely following oral exposure to the BSE agent.

The majority of people with sporadic CJD and all the people diagnosed with vCJD who have been tested, have a particular form of the PrP gene that is found in 40% of the UK population. This genotype probably makes PrP^C more vulnerable to conversion into the abnormal form associated with disease. In July 2004, a patient with a different form of the PrP gene had vCJD infection detected in their spleen and one cervical lymph node during a post mortem. The patient had died from a cause unrelated to vCJD. This was some years after a transfusion of non-leucodepleted red blood cells from a donor who later developed vCJD. The patient had not become ill with vCJD and it is unclear whether they would ever have done so.

11.4 Transmission of vCJD

Prion diseases are transmissible in certain circumstances, but they are not infectious in the usual way. They are not spread by respiratory droplets, direct skin contact or sexual contact, nor is there evidence of mother-to-child transmission.

In vCJD the consumption of BSE-contaminated beef or other bovine-derived products remains the most likely means by which vCJD was acquired, and to which most of the UK population would have been exposed. Other sources of vCJD infection may include inoculation from contaminated medical equipment or infected transplant material. So far, there are no recorded instances of vCJD being spread through surgery, nor have there been any cases amongst recipients of plasma products sourced from individuals who later developed vCJD. However the recent (July 2004) announcement of the second case of transmission of vCJD infection after receiving a blood transfusion from a donor who themselves died of vCJD increases concern about the possible infectivity of blood.

There is no epidemiological evidence that transfusion of blood from people with sporadic CJD has resulted in transmission of infection. However, experiments in which blood from humans with sporadic CJD is injected intra-cerebrally into animals suggest that blood may contain infectivity, albeit at a relatively low level, and some cases could have occurred without this source being recognised. Experiments in several animal models have shown that blood from an animal infected with a TSE can be infective when inoculated intra-cerebrally into the same species. An on-going experiment in sheep has shown transmission of experimentally induced BSE via blood transfusion. Other evidence suggests that infectivity of blood from animals that are infected but asymptomatic is less than when symptoms develop.

12. Sources for Additional information

The process of informing patients about their possible additional risk status, and the special precautions they may need to take is being coordinated by the Health Protection Agency (HPA) in England, Wales and Northern Ireland, and in Scotland by the Scottish Centre for Infection and Environmental Health (SCIEH).

More information about vCJD with useful links is available from their websites
HPA: http://www.hpa.org.uk/infections/topics_az/cjd/menu.htm
SCIEH: http://www.show.scot.nhs.uk/scieh

Further information is also available from:

National Public Health Service for Wales
http://www.wales.nhs.uk/sites/home.cfm?OrgID=368

Transmissible spongiform encephalopathy agents: safe working and the prevention of infection. Guidance from the Advisory Committee on Dangerous Pathogens and the Spongiform Encephalopathy Advisory Committee. 1998 and 2003. http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/

CJD Incidents Panel
http://www.hpa.org.uk/infections/topics_az/cjd/incidents_panel.htm

Det Norske Veritas vCJD blood risk assessment
http://www.dnv.com/consulting/news_consulting/RiskofInfectionfromvariantCJDinBlood.asp

National CJD Surveillance Unit, Edinburgh http://www.cjd.ed.ac.uk/index.htm

National Prion Clinic www.st-marys.nhs.uk/specialist/prion/index_prion.htm

CJD Support Network http://www.cjdsupport.net/

Human BSE Foundation http://www.hbsef.org/

Spongiform Encephalopathy Advisory Committee http://www.seac.gov.uk/

Department for Environment, Food and Rural Affairs BSE home page
http://www.defra.gov.uk/animalh/bse/index.html

CJD Therapy Advisory Group guidance
http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/CJD/CJDGeneralInformation/CJDGeneralArticle/fs/en?CONTENT_ID=4032403&chk=LVJY6b

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CAL.map
8th Oct, 2004

Mr GRO-B
GRO-B
GRO-B
GRO-B

Dear Mr GRO-B

Re : Variant Creutzfeldt-Jakob Disease and Plasma Products

In response to your reply letter dated ..19/9/.. we confirm that you / ~~your child~~ did / ~~did not~~ receive an implicated batch.

You ~~have~~ / have not requested an appointment to discuss the implications of this issue.

Yours sincerely,

GRO-C
Dr Simon Brown
Consultant Haematologist

GRO-C
Christine Harrington
Nurse Consultant