

SNBTS DOCUMENT REQUEST No:

2011/00095

DR RUTHVEN MITCHELL

PENROSE INQUIRY TOPIC B2 – REQUEST FOR INFORMATION

1. With reference to documents SNB.007.0860 (letter from Dr Davidson to Dr Wallace dated 9 June 1976) and SNB.007.0970 (letter from Dr Hopkins to Mr Watt dated 22 December 1976) can Dr Mitchell remember whether “rationing” was in operation when he became Regional Director for Glasgow and the West of Scotland Blood Transfusion Service in 1978?

In 1978 there was a system of allocation of PFC Factor VIII which was arranged centrally and based upon a series of formula which did not entirely satisfy those concerned:-

- (a) Allocations depended on the amount of grams of fresh frozen plasma sent to the PFC from each region (over 20 tonnes according to Medicines Inspectorate Report March 1982, reference 000/59) and at the same time the final product produced by the PFC depended on the yield, the potency, the purity and the ease of use. These criteria did vary from time to time and it was difficult to pin the PFC director down to the criteria for the final product. At times this was disheartening and the allocations were not always equitable, resulting in inevitable competition for stock in the various regions;
- (b) Allocation depended on usage in each region in terms of haemophilia coagulation units. This fluctuated with measurement of the coagulation unitage of the various Factor VIII products and attempts were made to allocate stocks on the basis of the number of Factor VIII coagulation units sent to the PFC from each region as fresh frozen plasma and latterly as recovered plasma. When self-sufficiency was achieved there was no need for any restriction but my despatch staff were noting that there was not a large uptake of Factor VIII from the PFC. In addition, to avoid unnecessary delay from the time of donation until the time of separation and freezing of the fresh plasma, a delay interval of no more than about eight hours was agreed. That is the reason that the advent of the mobile laboratory and the mobile collecting centres in the Glasgow and West of Scotland region was extremely important in arranging on-site freezing capability in distant locations, for example Oban, where collection teams might remain overnight (see reference 2010/00028);
- (c) Allocation depending on the number of patients in each region always seemed to be a more sensible system per head of population. There could be unexpected demands for emergency admissions and surgical procedures and the aggressiveness of management of patients, for example the introduction of home therapy had to be taken into account. Clearly the clinical demand in each region would vary according to local practice, again giving rise to competition for available stocks;
- (d) Because of some of these problems gradually increasing national figures of 1m, 2m, 2.5m and 2.75m units per million of the population were agreed, with the 2.75m figure being agreed at the regional transfusion directors and haemophilia directors meeting on 21 January 1983 and each regional haemophilia unit made their requirements known centrally.

Certainly in the West of Scotland this was not made known to the regional transfusion centre which acted merely as a transport mechanism between the PFC and the individual haemophilia units in the region.

I did not see the letter nor the reply or replies between Dr Davidson and Dr Wallace nor between Dr Hopkins and Mr Watt at the PFC in 1976 but I was aware that commercial products Factor VIII were being purchased. It is unusual for Dr Davidson to have used the word rationing since it was merely a question of how much material the PFC had produced and what was sent to individual Haemophilia Centres according to their needs. The actual stock holdings and deliveries are now not known to me but I am sure they would be available in the stock control documents at the Protein Fractionation Centre. Unfortunately, as I understand it, all of the West of Scotland documents have been destroyed.

It is to be remembered that the PFC opened in 1975 and prior to that the principal treatments for haemophilia as far as I recall would be cryoprecipitate and fresh frozen plasma together with commercial product. Cryo and FFP would suffer from problems of volume and the commercial product would be used for larger bleeds where a larger more concentrated form of Factor VIII would be required. Later as the needs changed in line with practical and more aggressive treatment using increased amounts of Factor VIII and Factor VIII of higher potency, requirements of the PFC for fresh plasma became more demanding. In March 1981 the target figure of 2.75 million units per million population was decided and the drying plant at Law Hospital closed in December 1982, which meant that additional supplies of plasma could be sent to the PFC, which had otherwise been used for the production of single unit cryoprecipitate and fresh frozen plasma.

When regular meetings were held between SNBTS and haemophilia clinicians in around 1981 there was a recognition that increased demand meant increased collection of fresh plasma for the PFC and the goal of self sufficiency became desirable, mainly for safety reasons. Such cooperation through 1981 and right through to 1985 gradually built up a compilation of haemophiliac patients, their degree of clinical severity and their anticipated requirements. This was not immediately achieved because PFC, in attempting to make heat treated Factor VIII, had to sacrifice some of the amount of yield taken from raw plasma coming from regions. In addition there was a recognition that dedicated batches of Factor VIII were desirable and home therapy prophylaxis was becoming popular.

This steady relentless pursuit of abundance for all became a moving target. The allocations of Factor VIII made to the individual regional haemophilia centres were based on what Haemophilia Directors assessed their needs to be and had been identified through the formed haemophilia register, which became finally usable by 1984. Nevertheless even this would only cope with the regular management of patients, and provision had to be made for unexpected demand because of the more serious incident of haemorrhage. These steps were progressive through the 1980's which also had to anticipate the increase in life expectancy of haemophilia patients and the advent of more aggressive elective surgery. Much of the progress was due to the efforts of Professor Cash in his discussion papers on the trends in the management of haemophilia. Whilst the regional supplies were being allocated centrally, sufficient reserve stocks had to be kept at the PFC where more and more work was being done to improve the products which, although improving, could only provide purity or potency at the expense of the total amount of fresh frozen plasma sent from Regions. For example, to produce long term heat treatment at 24 hours exposure to 68 degrees celsius meant a loss of between 15 and 20% of the Factor VIII. All regions therefore had to respond and, in the West, increased amounts of

fresh frozen plasma were collected by the introduction of the mobile donating centres and the mobile laboratory, where freshly collected and separated plasma could be frozen at -80 degrees celsius. This became a welcome addition to the need to make up the losses of donor collection areas due to industrial recession to which I have already commented. From the papers available to me the timescale appears to be:-

Pre 1974 cryo and FFP plus commercial.

1975 PFC opens.

June 1976 Dr Davidson letter to John Watt.

December 1976 Dr Hopkins letter to John Watt at PFC - PFC records could be searched for quantities of plasma received and amounts of Factor VIII produced.

March 1981 target of 2.75 million units agreed.

December 1982 Law Drying Plant closes.

January 1983 target figure agreed and confirmed. Dr Ludlam asked for a "cushion" for PFC product during production of heat treatment and any losses.

March 1983 heat treatment trials and completion of haemophilia register.

November 1984 haemophilia register available by May 1984.

May 1985 batch dedication and increased heat treatment at 68 degrees celsius for 24 hours with reduced yield and higher virus kill.

2. With reference to document SNB.001.7242 (letter from Mr Watt to Dr Prentice dated 12 January 1978), was Dr Mitchell aware of the purchase of commercial product in the West of Scotland in 1977?

Although I did not see the letter from Mr Watt to Dr Prentice of January 1978 I was aware that commercial Factor VIII was purchased in the West of Scotland and elsewhere in Scotland and the United Kingdom.

3. Please see document SNB.007.1634 (letter from Dr Crawford to Mr Watt dated 24 April 1981) in which Dr Crawford refers to Dr Davidson's policy of rotating commercial suppliers. Was Dr Mitchell aware of this rotation policy and if so, does he have any comments?

I would see Dr Crawford's letter to Mr Watt about the Glasgow Royal Infirmary rotation of commercial suppliers of anti-haemophilic coagulant because when I became director all major correspondence going through the Centre was copied in to the "morning file" which circulated each day among the senior medical and technical staff. I therefore believe that Dr Crawford's comments concerning Dr Davidson's motives are, and were, accurate. I did not see any reply to Dr Crawford's letter and the PFC letter which was referred to Mr Watt does not show any action being taken. Nevertheless labels and packaging were changed to make the product more attractive to users and I am sure Dr Perry will have the details of when the labelling and package measurements were changed.

4. Did Dr Mitchell have any personal involvement in attempts to secure an adequate supply of PFC material for hospitals in the West of Scotland (i.e. the haemophilia centres at Glasgow Royal Infirmary and Yorkhill) in the period from 1978 to 1983?

My involvement in procuring Factor VIII for the West of Scotland was not direct since haemophilia units made their requirements known directly and centrally to the Protein Fractionation Centre and the National Medical Director. My focus was in achieving the national targets for self-sufficiency in plasma procurement whilst maintaining the production of fresh frozen plasma, cryoprecipitate and dry plasma prior to the closure of the plasma drying plant at the Law Centre. Based on estimates of regional and national demand for Factor VIII, stock was sent to the regional transfusion centre via the PFC transport carrying other products from PFC. Thereafter products were delivered from the regional transfusion centre in the west to Glasgow Royal Infirmary and any other haematologist requesting any blood product. Every haematologist in the West of Scotland had a copy of the booklet "Notes on Transfusion" and was aware of the formulation of the various products available at the regional centre produced by the Protein Fractionation Centre. Reconstituted Factor VIII for patients in Wards 2 and 3 at Glasgow Royal Infirmary were made available via the coagulation laboratory attached to the Haematology Department at Glasgow Royal Infirmary under the control of Dr Davidson and Dr Isobel Walker.

5. What does Dr Mitchell remember about the use of commercial product at (a) Glasgow Royal Infirmary and (b) Yorkhill?

I recall commercial Factor VIII being regularly used at Glasgow Royal Infirmary and Yorkhill Hospitals but cannot say when the practice ceased or when their needs were satisfied by provision of 100% PFC product, although at that time it was clear that the National notional target of 2.75m units per million of population (SNB.001.5162) had been achieved.

6. Does Dr Mitchell remember any concerns being expressed to him by haemophilia clinicians in the West of Scotland regarding (a) quality of PFC product or (b) the security of its supply?

I was aware that clinicians had experienced problems with solubility of PFC Factor VIII as well as some allergic reactions and that PFC was aware of these in trying to improve solubility and efficacy. I was also aware that clinical requirements were ever-changing and that previously agreed targets became moving targets and always subject to an upward demand rather like catching quicksilver.

In my professional experience I have seen the transition in the treatment of haemophilia from fresh plasma through a variety of ever-increasing potent and efficacious Factor VIII concentrates and for clinical use.

Ruthven Mitchell

9 August 2011