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MINUTES OF THE MEETING OF DIRECTORS OF THE SCOTTISH NATIONAL BLOOD TRANSFUSION SERVICE AND HAEMOPHILIA DIRECTORS HELD IN ST ANDREW'S HOUSE ON FRIDAY, 21 JANUARY 1983

Present:

Dr A E Bell (Chairman)
Dr B Bennett
Dr Ewa Brookes
Dr J D Cash
Dr C D Forbes
Profensor R H Girdwood
Dr C A Ludlam
Dr R Mitchell
Dr D B L McClelland
Dr G A McDonald
Dr C R M Prentice
Dr T G Taylor
Mr J C Watt

In attendance:

Dr A D McIntyre, SHHD
Mr K A M McBryde, SHHD
Mrs M J Learmonth, Secretariat

Apologies for absence:

Apologies for absence were received from Dr Tudhope, Dr Lewis, Dr Urbaniak, Dr Dawson and Dr Willoughby.

1. Chairman's Remarks

The Chairman welcomed members, particularly Dr Brookes who was attending for the first time and Dr Taylor from Inverness. Dr Bell also wished Dr Prentice well in his new appointment in England; it was intimated that Dr Forbes had been appointed to succeed him as Haemophilia Co-Director at Glasgow Royal Infirmary.

2. Approval of Minutes

The Minutes of the meeting of the Group held on 30 January 1981 were approved.

3. Matters Arising

Dr Bell said that most of the issues arising from that meeting had been taken up by the Working Group set up under the chairmanship of Dr McDonald and would be discussed under items 4 and 5 of the Agenda. It was however reported that, following discussions between the Department and other interested parties, agreement had been reached that Edinburgh and Glasgow would be recognised as Haemophilia Reference Centres with the same title and standing as those in England and Wales. It was appreciated that the single tier regional responsibilities of Haemophilia Centres in Scotland differed from those in England and Wales, and that the referral of patients was at the discretion of each Centre and on an ad hoc basis. It was agreed that there need be no problems over supplies of factor VIII for patients who might have to travel outwith their own area, since arrangements could be made for the transfer of blood products.

4. The Chairman invited Dr Cash to introduce the paper which he had prepared to facilitate discussion with regard to future SNBTS planning for the production of blood products required for patients with haemostatic or thrombotic problems, and indicated that discussion arising from the paper would cover items 5(i) to 5(v) of the Agenda.

(a) Trends in Supply and Demand for Factor VIII Concentrates.

Figures quoted for the 5 year period 1978 to 1982 showed that:

(i) there had been a sustained increase in the total amount of fresh plasma processed, although it was anticipated that the increases would probably now level out, unless there was significant further financial investment at the Regional Transfusion Centres.

(ii) there had been a decrease in the amount of cryoprecipitate issued from the RTCs; and

(iii) there had been a substantial increase in issues of the PFC intermediate factor VIII concentrate.

Dr McDonald congratulated the SNBTS Directors and the PFC on the quantity and quality of factor VIII concentrate being produced, and also paid tribute to clinical colleagues who had used a greater proportion of red cell concentrates rather than whole blood.

At the last meeting a target figure for the amount of factor VIII which would be required in the next 5 years was proposed as 2.75 iu x $10^6/10^6$ pop per annum. This target figure had been agreed by the Working Group as a reasonable assessment of demand, and after discussion was adopted by the meeting as a firm recommendation.

Concern was again expressed about the amount of commercially produced factor VIII which was still being purchased and members went on to discuss the regional breakdown of the usage of cryoprecipitate, PFC concentrate and commercially produced factor VIII. It was noted that while purchases of commercial VIII had declined in Glasgow, purchases in Edinburgh had increased. Dr Ludlam explained that the reasons for the use of commercial material in Edinburgh were partially clinical, and partially a policy of conserving a cushion of NHS VIII against an anticipated shortage when production at the PFC would be suspended to carry out alterations required by the Medicines Inspectorate.

In reply to questions about the effect of the PFC refit on supplies, Mr Watt said that although it was difficult to predict the problems which might arise at the downtime, the PFC at present issued 2,000-3,000 vials of factor VIII per month and at the present rate of uptake 6 months supply is held. Fears of a shortage were remote and he was confident that, with cooperation between regions, difficulties could be overcome. Dr Cash emphasised that the pro rata system was not intended to be applied inflexibly and that products could be transferred between regions in the event of a local shortage.

The Chairman stressed that the SNBTS had been set up to have the capability to cope with all Scottish requirements, other than those few therapeutic agents the production of which might not be justified on a very small scale, and that in terms of national policy the purchase of commercial products should be avoided so far as possible. Dr Ludlam also expressed some misgiving that Edinburgh perhaps did not receive as much PFC factor VIII concentrate as it should pro rata. It was remitted to Dr Cash, Dr McClelland and Dr Ludlam to resolve any problems which had arisen in relation to supplies to Edinburgh.

(b) Freeze Dried Cryoprecipitate (FDC)

Dr Cash expressed SNBTS thanks to those who undertook the successful clinical trial of this product in the west. Notwithstanding this work, it had been decided to

abandon production of FDC meantime, having regard to the closure of the plasma freeze drying plant at Law and the cost of meeting the standards demanded by the Medicines Inspectorate. The prospective availability of a hepatitis risk reduced factor VIII concentrate also cast uncertainty over the future of FDC at the present time.

(c) SNBTS Factor VIII Study Group

This active study group set up in 1982 was engaged in examining ways of improving the quality of fresh frozen plasma which arrives at PFC. Progress was encouraging and significant benefits were anticipated within the next 3 years.

(d) Higher Purity Factor VIII Concentrate

Following a request made at the last meeting of Haemophilia and BTS Directors efforts had been made to provide a factor VIII concentrate with a low fibrinogen content. It was gratifying that a new method had been developed and was currently subject to a patent application. It was anticipated that small amounts of this product would be released for limited clinical trials later in the year.

(e) Heat Treated Factor VIII Concentrate

Associated with the foregoing development the PFC was also going ahead with the development of a heat-treated product with reduced risk of transmitting hepatitis. However concern was expressed about the commercial firms who were anxious to capture the market for their own heat-treated product, and by offering supplies of their material for clinical trials might preempt the available suitable patients before the PFC product was ready for similar trials. Mr Watt explained the problems which had to be overcome in preserving acceptable yields and providing a product which was not too expensive, considerations that were of less importance with the commercial product. Directors were made aware of the fierce competition facing the PFC from commercial concerns and were asked to bear in mind the stated policy for the Scottish Health Service to be self-supporting in blood products. The PFC would have limited amounts of heat-treated factor VIII available for trials in the

near future, and haemophilia directors agreed to support the PFC as much as possible in the development and clinical trials of the NHS product. It was agreed that the Working Group should keep these developments under review and help to promote whatever collaboration was required to bring the PFC heat-treated factor VIII most effectively into therapeutic practice.

(f) Factor IX Concentrates

The supply position of DEFIX over the last 5 years had remained strong and the demand reasonably stable. The clinical studies undertaken on the development of Supernine had produced excellent results, thanks being due to Dr Boulton as well as colleagues in the haemophilia centres in Edinburgh and Glasgow. It was not thought necessary to obtain a separate product licence for Supernine, a variation of the DEFIX licence on a named patient basis being considered sufficient.

The withdrawal of DEFIX from PFC's production range had been considered, but this was now regarded as premature until further studies had been completed in relation to new products for the management of haemophilia A with inhibitors.

It was reported that studies of heat treatment, to reduce the hepatitis risk, were currently under way using Supernine. However the rate of progress with this product would be slower than with factor VIII because of the necessity to submit the heated IX concentrate to intensive animal studies in order to confirm that the heat treatment had not resulted in a thrombogenic product.

(g) Factor VII Concentrate

Significiant progress towards the production of a factor VII concentrate had been achieved. Dr John Davidson had kindly agreed to collaborate with Dr Cash on the clinical evaluation of this product after it has been animal tested.

(h) Antithrombin III Concentrate

Dr Cash reported that the overseas data on research into this product was not entirely convincing. He felt that caution was required and that promotion of clinical research in this area within the SHS was desirable. Mr Watt agreed that this project was low priority at the present time, with possible development in 1984/85.

The Chairman and members expressed their appreciation of Dr Cash's paper, both for its information and as a framework for discussion. Dr Cash said he would be willing to provide similar documents for future meetings.

5. (a) Determination of quantities of Factor IX Concentrate used for Haemophilia B and non B patients

Dr McDonald reported that the Working Group had still to give this item further consideration.

(b) Reporting of adverse reactions

Dr McDonald reported that the Working Group had discussed this matter which was still under consideration. Dr Cash had recently consulted the Scottish Consultant Haematologists' Group for their views and efforts were being made to draft a reporting form specifically for adverse reactions to blood products, which would be acceptable to the various interests concerned. Dr Crawford had undertaken to produce a document for consideration by transfusion directors in the first instance.

In the meantime clinical colleagues were being reminded of the importance of reporting adverse reactions. The legal duty to ensure reporting of incidents was also stressed.

(c) Haemophilia Register

The Working Group had discussed this question on two occasions and reached the conclusion that it would be inadviseable to adopt a system requiring major resource commitment at haemophilia centres. Dr Ludlam had approached ~~by~~ Dr Rizza to see if it were possible to extract Scottish data from the computerised Oxford Haemophilia Register. Dr Rizza had completed this exercise and produced print-outs of the Scottish data. Dr Ludlam and other directors expressed the Group's appreciation of this collaboration from Oxford. It was noted that the information from Oxford broadly confirmed the assumptions made in Scotland from the amount of therapeutic material issued. There were nearly 400 haemophiliacs registered for Scotland, which represented 8 to 9% of the UK total; the figures by age and severity showed that there were fewer very young patients in Scotland.

It was felt that although the information received went some way towards Scotland's needs for management purposes (and met the basic recommendations of the Council of Europe) it was unfortunate that there was no breakdown of the figures for the Scottish regions. It was agreed in discussion that regional information should be ascertainable within the professional framework of exchange between colleagues, while maintaining individual patient confidentiality, and that the Working Group should continue to pursue the matter in this context.

(d) Hepatitis

Developments in relation to hepatitis had been covered in discussion of heat-treated coagulation components, and hepatitis would remain on the agenda of the Working Group.

6. (a) Acquired Immune Deficiency Syndrome (AIDS)

Dr Cash drew members attention to recent articles in the United States, and also in the Observer and the Lancet, about this problem. A MMWR extract (CDC, Atlanta) had been circulated with his paper. Dr Ludlam informed members that in the UK a letter and questionnaire had been sent out to haemophilia directors.

(b) Packaging (Note tabled by Dr Cash)

Dr Cash informed members about consultations which had been undertaken by Dr Boulton on the packaging of PFC materials. It had emerged that there was agreement that the existing packaging was too bulky. Recommendations for changes in this and other related matters would be made to the PFC.

Dr Brookes also asked members' views on the inclusion of a coarse filter needle in packs. Mr Watt explained the reasons for exclusion of the needle, but noted that if it were required a change in practice would be in order.

(c) Epileptiform attacks (Note tabled by Dr Cash)

Dr Cash reported that between September 1982 and January 1983 occurrences of epileptiform attacks had been reported by Dr C Forbes in 2 patients after

receiving factor VIII infusions. The matter is under investigation and it is not possible to arrive at conclusions yet. However the incidents and their investigation highlight the importance of immediate and detailed reporting of adverse reactions so that prompt action can be taken in the recall of suspect material.

(d) It was agreed that representatives from Northern Ireland should be invited to attend future meetings.

7. Future meetings

It was agreed that the Working Group should continue to meet as required. Dr McDonald agreed to continue as Chairman and approval was given to the co-option of additional members ad hoc for the discussion of individual items of business.

The next meeting of the full Group would take place on Thursday, 2 February 1984.

Scottish Home and Health Department
March 1983