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JDC/MAC

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Dear John

FFP / PFC / FACTOR VIII

I thank you for the copy of your interesting letter of 9th January to General Jeffroy on the above subject. I was extremely disappointed when, earlier in the year, your suggestion of providing an annual estimate for each region on the supply of FFP was rejected by your fellow Regional Directors. It is my own opinion that, even when wrong, it is useful to have a target pre-set in space and time toward which one can aspire. Rather sadly, when it comes to factor VIII concentrates, the achievements of the PFC have a habit of falling short on expectation. These failures arise partly within the PFC, partly due to my tendency to optimism and partly to the peregrinations of the plasma supply situation.

You and the staff of the Edinburgh Centre are to be congratulated on exceeding your estimate by a comfortable margin; if nothing else you have vindicated completely the policy of forward planning. In my opinion "doing ones best" would have to include some kind of estimate against which one can make a measure of whether or not best is really being achieved.

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I think one could split hairs on the subject of your numbers but there is one point on which, recently, I have been carrying out a serious assessment and that is the real yield of the PFC in terms of factor VIII concentrate. It is true that we are getting better at the game and are showing more uniformity of performance and that our crude yield is roughly 40% on average. However, I have recently been making rough calculations taking into account the amount of material removed from each pool for the various aspects of quality control. This, together with the losses occasioned on resolution leads me to believe that the actual yield at the point of administration to the patient is probably closer to 30% overall. Quite obviously one of our major and immediate future problems is to reduce and improve this situation. We have now completed the preliminary investigations of the concept of adding polymer to the plasma at the time of separation and I am preparing a series of vials of additive solution so that we can mount a trial of this concept through the good offices of Iain Cook. Early studies with PEG suggest that we may be able to protect AHF during storage and the early stages of processing and so reduce some losses. Equally, the second serious point of process loss, filtration, has been occupying our minds for some time and we now have quite good evidence that this loss is partly mediated by temperature but, perhaps more importantly, by the materials used for filtration. We now await supplies of a new type of medium which is expected to show substantial improvement. At least there is some German which is encouraging. These factors should all, I hope, upset your calculations in the right direction.

The letter which General Jeffroy wrote in August was based on the assumption that we could expect supplies of FFP to the PFC to be maintained at the levels achieved in early 1975 but this assumption was a disastrous error since the plasma intake to the PFC is now back to the levels of 1972 or thereabout. The record for 1976 so far is that we have processed one pool (roughly 120 doses) and have allocated process space for a second pool in the first week of February although I have not allocated a pool number since the plasma is not to hand. In November and December 1975 we had allocated space for 16 batches of AHF but 12 of those had to be allocated to cryoprecipitate supernatant to keep my staff in employment and in an attempt to "scrounge" a little extra active material. This process yields between six and 20 vial units containing not less than 250 units of factor VIII which could be redissolved in 100 ml but which contains 3.2 g of protein per dose. I know that this is not a very wonderful product but I believe it to be capable of improvement and it does represent, in terms of the amount of cryosupernatant in store, a potential of almost 6 000 000 units.

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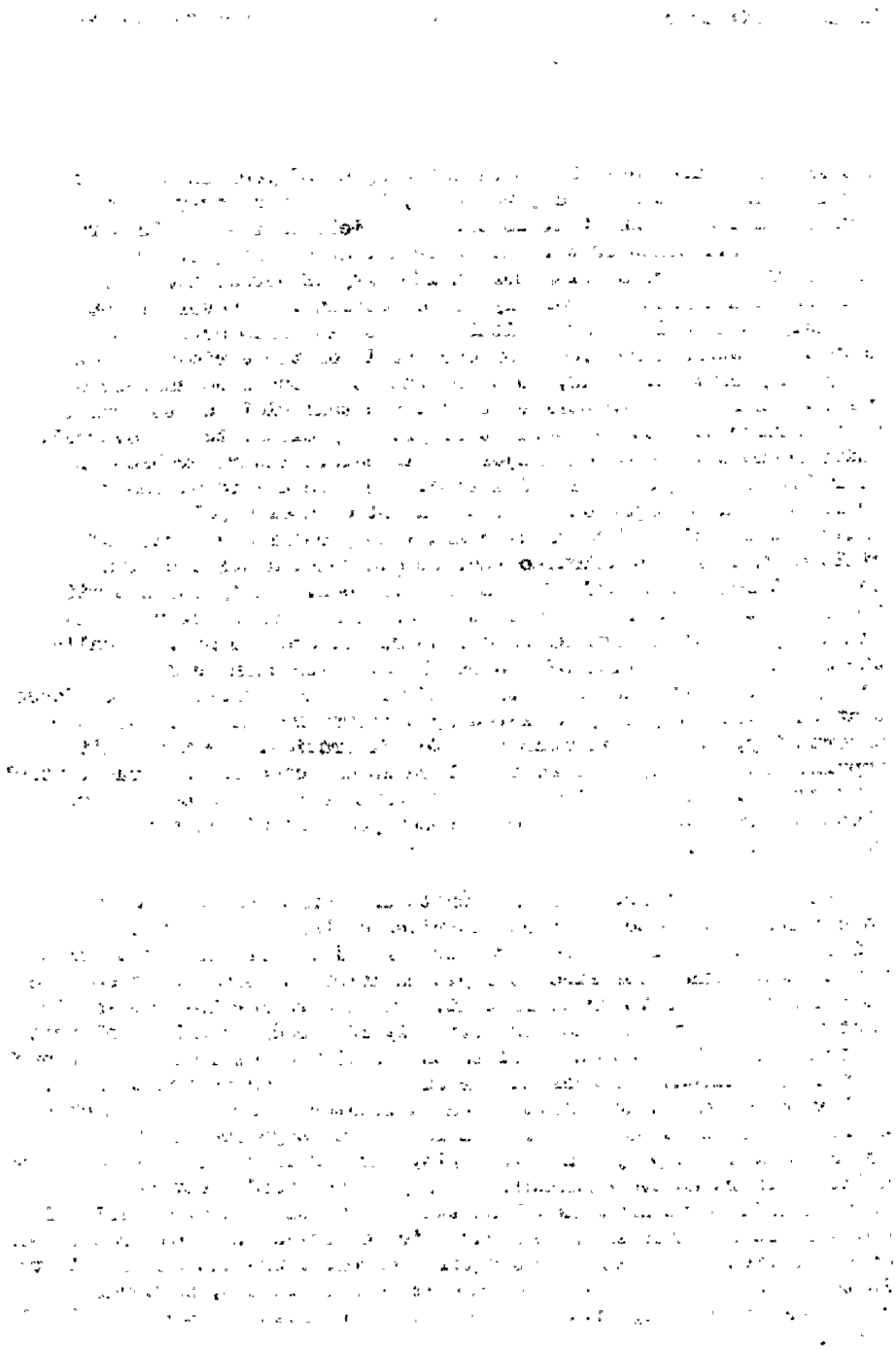

I would like to believe that the PFC will be able to support the very creditable estimate you have made forward into 1977 but I believe that the realistic answers to the questions in your last paragraph are that, unless present patterns of plasma supply change dramatically, you can expect the current trend of falling issues to continue with a leveling of the curve about the level of weekly delivery which you suggest. The "missing vials" have gone to your colleagues in other regions and I doubt if reimbursment is possible. One alternative is the suggestion that each region sends to the PFC such fresh plasma as is considered necessary for the return of intermediate concentrate to that region. If this policy were adopted then most of the production from Liberton would go to Edinburgh and Inverness pro rata. You know well my opinion of such a policy but if you were to make such a suggestion I think that, under present circumstances, I would feel bound to give you my full support. I do not believe that this is the correct way to tackle a national problem but it may be the only solution in face of the failure of the policy of communality of regional effort. Perhaps the answer lies in the last sentence of your letter which, in itself, poses another question "which patients?".

With kind regards

Yours sincerely

JOHN G WATT
Scientific Director

c.c. Major-General H C Joffrey