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PAPER VI

Implications of AIDS for production of FVIII at BPL

1. BPL manufactures an intermediate purity FVIII concentrate.

2. This year BPL will process approximately 130,000 litres of fresh plasma (FFP) to produce approximately 26 million i.u. FVIII. There is capacity in the existing factory to process approximately 150,000 litres of plasma (30 million i.u. FVIII).

3. Regional Transfusion Centres produce a variable quantity of single-donor cryoprecipitated FVIII. On average, each Region produces about 10,000 bags of cryoprecipitate (equivalent to approximately 1 m i.u. FVIII) per Region. One or two Regions have traditionally produced rather more cryoprecipitate than the majority - say 17-19,000 bags.

4. The more cryoprecipitate a Region produces, the less plasma it can send to BPL for FVIII concentrate production.

5. The major advantage of cryoprecipitate is that each bag comes from a single donor. Although an episode of bleeding may require a total of, say, 100 bags of cryoprecipitate (equal to 100 donors), every vial of FVIII concentrate is derived from a pool of plasma from 500 (PFL, Oxford) to 3,000 (commercial) donors. The pool size for BPL is approximately 1-1,500 donations. Exposure to fewer donors is thought to reduce the risk of infection to those receiving cryoprecipitate rather than concentrate.

6. There is some evidence from the USA to suggest that asymptomatic haemophiliacs who had been treated with FVIII concentrates were more likely than those treated with cryoprecipitate to have abnormal ratios of T-helper and suppressor lymphocytes, suggesting some disordered state of immunity in the patients receiving FVIII concentrate but not in those treated with cryoprecipitate. These results (N Eng J Med 1983, 308, 83-86) must be interpreted with caution. In particular, it should be noted that the cryoprecipitate was derived from volunteer plasma whereas the concentrate came from paid plasmapheresis donors. Nevertheless, the signed leading article in the same edition of the journal (pp 94-95) advocates the need to consider a change to a greater use of cryoprecipitate "even though we may not have enough evidence to demand such a radical change". It should also be noted that in Dr Gunson's summary of the Council of Europe Meeting on AIDS, he discerned a trend towards encouraging the greater use of cryoprecipitate in Europe (see paper II p. 4).

7. There are a number of disadvantages to cryoprecipitate as therapy for haemophilia, particularly for home treatment.

   i) It has to be stored deep frozen (concentrate can be stored in a domestic refrigerator).

   ii) It is messy to make up and inject and there is more difficulty preventing contamination during thawing and pooling.

   iii) Considerable volumes may be needed requiring i.v. infusion rather than injection.

   iv) It frequently causes allergic reactions.

   v) It is more difficult to calculate the dose required as the number of units of FVIII per bag is not known accurately.

8. In certain European countries a freeze-dried (rather than frozen) cryoprecipitated FVIII product is manufactured. Such material can be stored in a domestic refrigerator. There is little advantage in terms of donor exposure where the national product (as in Belgium) is large-pool freeze-dried cryoprecipitate. Small-pool (say 12 donor-pool) freeze dried cryprecipitates suffer high losses of product during quality control procedures and may be expensive to produce. No country has yet used repeated plasmapheresis of "accredited" donors to produce a moderate pool-size product (say 500 donations) from a smaller number of donors (say 50), thus combining the production advantages of a larger pool with a smaller donor exposure.

9. At present, haemophilia centre directors in the UK are not advocating a change in the pattern of treatment of haemophiliacs which would require increased production of cryoprecipitates. However, this could well change if a haemophiliac who had received only BPL concentrate were found to have developed AIDS.

10. If there were to be a significantly increased demand for cryoprecipitate, this would pose major operational and financial problems for RTCs and would reduce significantly - or even totally - the amount of plasma sent to BPL. The alternative to single donor cryoprecipitate produced in RTCs would be for BPL to change to small-pool freeze-dried cryoprecipitate production. The operational problems posed by such a switch in technology would be immense and it is doubtful whether it could be undertaken in the existing facilities. Moreover, the design brief for the redeveloped BPL would have to be totally re-worked to plan for the changed requirements.

11. The preceeding paragraph describes a worst-case situation. Nevertheless, the demand for cryoprecipitate could well increase to a certain extent and we need to know what contingency plans the CBLA has - or is in the process of developing - to deal either with a reduction in the supply of plasma to BPL or with conversion of part of its manufacturing out-put to freeze-dried cryoprecipitate.

12. Ascertaining the views of the CBLA could be either by

    i) a specially convened DHSS/CBLA meeting, or

    ii) Dr Harris could ask for it to be dealt with as an agenda item, for which DHSS could provide a paper.

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