

OPTIMUM USE OF FACTOR VIII PREPARATIONS AT PRESENT
AVAILABLE IN THE UNITED KINGDOM

1. In this paper the experience and conclusions of the staff of the Newcastle Centre where three factor VIII preparations are used in the treatment of haemophilia are presented. The preparations are:-

Cryoprecipitate	(Newcastle Regional B.T.S.)
'Hemofil'	(Travenol Laboratories)
Fresh Frozen Plasma	(Newcastle Regional B.T.S.)

2. Present practice in Newcastle:-

Cryoprecipitate is used for the treatment of

- i. outpatients attending the Centre with bleeds,
- ii. inpatients with bleeds,
- iii. patients undergoing surgery or dental extraction, and
- iv. patients receiving physiotherapy and mobilisation following bleeds.

'Hemofil' is used in

- i. the home therapy programme,
- ii. the management of severe bleeds when insufficient cryoprecipitate is available,
- iii. the management of some patients with antibodies and
- iv. the management of those patients who experience severe reactions to cryoprecipitate or fresh frozen plasma.

Fresh Frozen Plasma (F.F.P.) is used in

- i. adults with mild to moderately severe bleeds when no cryoprecipitate is available, and
- ii. adults with mild to moderately severe bleeds when cryoprecipitate has to be reserved for use either in children, or in adults with severe bleeds or following surgery.

3. Statistics:-

Patients The distribution of patients by diagnosis (March 1974) in the Newcastle Region is:

Haemophilia A	severe	80
	moderate	35
	mild	48
	awaiting assay	7
	Total	170
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Von Willebrand's Disease		52
Haemophilia B (Christmas)		21
Other factor deficiencies		12
Awaiting specific diagnosis		35
Potential carriers identified		234
Known carriers		100
	Total	624

*Population
of Region*

Of these patients those with haemophilia A, von Willebrand's Disease and a minority of haemophilia A carriers require cryoprecipitate or concentrate. Those with haemophilia B require IX concentrate and those with other factor deficiencies sometimes require F.F.P. Cryoprecipitate, F.F.P. or fibrinogen concentrate are required for patients with acquired factor deficits, and F.F.P. is used in occasional cases of angio-neurotic oedema.

Of the 170 known haemophiliacs (A) in the Region 43 regularly attend the Newcastle Centre with acute bleeds. All haemophiliacs requiring surgery, dental extraction or the management of complications attend Newcastle.

Products

Cryoprecipitate

Approximately 14,000 packs of cryoprecipitate are prepared and issued by the Newcastle Regional B.T.S. per annum.

Of these 60% are used at the Newcastle Haemophilia Centre and 40% at other Regional Hospitals.

'Hemofil'

Expenditure on commercial concentrate will be approximately £20,000 in the first year of use in Newcastle. 23 patients with severe haemophilia A are now on the home therapy (H.T.) programme, and account for the bulk of this supply.

On average each H.T. patient uses 5 vials of 'Hemofil' per month (cost £128/month; £1,536/year).

Within the Region 'Hemofil' is only issued by the Newcastle Centre, patients suitable for H.T. being trained there and having to visit the Centre for renewal of stock on presentation of accurate records. Regional sub-centres may receive small stocks of commercial concentrate for emergency cover through Newcastle.

A monthly audit of supplies is performed by the Finance Department and the Sister responsible for the H.T. programme.

F.F.P.

Approximately 800 packs of F.F.P. are prepared by the Regional B.T.S. per annum. 204 packs have been used in the management of haemophilia in Newcastle in the past year.

4. Comparison of Products

Cryoprecipitate

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Until this year it has not been possible to perform regular assays on pooled cryoprecipitate in Newcastle. Assays on random packs have indicated a very variable yield with an average of 70 units VIII per pack. Dosage has been determined by clinical experience rather than either assays or formulae. The majority of severe bleeds cease with the following regime:

F.F.P.

F.F.P. carries no real advantage to haemophilic patients and may be dangerous; circulatory overload will occur if it is used in the treatment of severe bleeds, reactions are frequent and acute allergic pulmonary oedema may complicate its use.

5. Conclusions

In preparing this paper we have been asked to consider ways in which present resources available to U.K. haemophilia services may be used to the optimum advantage of patients. In attempting this we must stress our conviction that the single most important factor in haemophilia management is the early recognition and immediate effective treatment of acute bleeding episodes. This means home therapy and the prescription to suitably trained patients of potent, small volume, lyophilised concentrate with which to treat themselves under the supervision of the Haemophilia Centres. We do not think that cryoprecipitate is a suitable material for home therapy, not least because so much would have to be stored in patients' homes in large scale programmes that there would be insufficient for the needs of inpatients at present production rates.

Any plan to conserve factor VIII containing blood products must take into account the fact that the majority of haemophiliacs are being undertreated. Therefore schemes to rationalise management on a Regional basis by improving the organisation of facilities will lead to increased rather than decreased or stabilized demand. This is not only because more patients will be encouraged to seek early treatment and will rightly demand home therapy, but because there exists a backlog of patients suitable for corrective orthopaedic surgery which has been denied them in the past because of poor organisation and lack of blood products.

However we do suggest that the following measures may be of benefit in the present economic situation:

- A. a Government campaign to educate the medical profession in the recommended use of blood products, stressing the importance of using red cells rather than whole blood for most clinical problems. To be most effective the campaign should be directed at surgeons and junior hospital doctors.
- B. a directive from the Department to all hospitals that patients with haemophilia presenting with problems likely to require surgery (however minor) or dental extractions, be referred to a Haemophilia Centre for treatment as early as practicable in the course of their illness. It is not unusual for patients to be referred after several weeks of conservative treatment in general hospitals, by which time prolonged factor replacement therapy is necessary. Seen early lesions can usually be treated with minimal therapy and considerable savings in bed occupancy and laboratory time.

In addition it should be widely known that the majority of haemophilic patients undergoing dental extractions are safely covered with one day of factor VIII replacement therapy together with anti-fibrinolytic treatment, and that where complete immobilization is possible (as after an orthopaedic procedure) factor VIII requirements are reduced considerably (from 2-3/52 to 4-5 days).

Children: infants	2 packs
1 - 5 yrs.	2 - 5 packs
5 - 8 yrs.	5 - 8 packs
Adolescents and Adults	8 -10 packs

Assays performed prior to major surgery show that at least 20 packs of the Newcastle product are required to raise the patient's VIII level to 40% initially.

The major disadvantage of cryoprecipitate is therefore the empirical dosage that must be employed. We purposely aim to give too much rather than too little and there is no doubt that wastage occurs as a result. However far more wastage occurs when small doses do not stop a bleed early in its development and we believe that this is the major reason for 40% of the available cryoprecipitate being used in hospitals other than the Centre.

The second disadvantage is the variability in supply, particularly during holiday periods. There is never enough cryoprecipitate to cover the needs of both acutely ill patients and the requirements for surgery, the gap being filled with either F.F.P. or concentrate.

'Hemofil'

In comparison with other products, 'Hemofil' was chosen for the H.T. programme for the following reasons:

- i. known dosage (units VIII activity/vial)
- ii. small volume
- iii. ease of preparation
- iv. ease of injection (syringe)
- v. low incidence side effects
- vi. ease of storage; no deep freeze needed, small bulk
- vii. less chance of contamination
- viii. use for travel/work away from home
- ix. long life before expiring.

Batches supplied since November 1973 have varied in potency from 230 units/vial to 290 units/vial. In planning the H.T. programme we decided to recommend an initial dose of only one vial provided that it was given at the first recognition of bleeding by the patient. The results of the first year of the H.T. programme will be prepared for publication later, but our impression now is that a small dose given at the start of a bleed will abort the bleed without the need for sustained therapy over a number of days. There is certainly a marked drop in out-patient attendances by H.T. patients and hospital admissions for non-surgical complications of haemophilia have fallen from 32 in the year prior to starting H.T. to 6 since starting H.T.* Only 2 of these admissions have followed haemarthroses, the remainder being for bleeding into neck, haematuria, head injury and abdominal pain.

* (Footnote) Comparisons will not be accurate until all patients reach 1 year on H.T.

- C. the restriction of use of expensive commercial factor VIII concentrates to recognised Haemophilia Centres. In our opinion home therapy programmes should only be run from those Centres where adequate supervision including regular checks on VIII antibody and H.A.A. status can be performed, and the patients use of concentrate carefully supervised. If the D.H.S.S. implement this proposal additional financial support will be needed by the Regional Health Authorities concerned.

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