AIMS

This is the third prophylactic study that we have undertaken at Alton. The first involved once weekly prophylaxis and the second twice weekly.

The aims of this Study were:-

1. To see if prophylaxis would improve the radiological appearance of joints and more particularly have any influence on haemophilic cysts.

2. To determine the optimum dosage.

PATIENT SELECTION

All patients selected had deteriorating joint and muscle function despite adequate on demand treatment, both at the College and their Home Centres.

SLIDES 8, 1, 3, 4, 6, 19

I have taken one patient to illustrate the joint and bone changes which we are interested in.

SLIDE 8 - Chronic haemophilic arthropathy of RIGHT KNEE.
Chronic effusion.
Overgrowth of femoral condyles.
Muscle wasting.
Square patella.

SLIDE 9 - Radiograph of RIGHT KNEE.

SLIDE 6 - Arthropathy of RIGHT ELBOW.

SLIDE 4 - Radiograph of RIGHT ELBOW - AD

SLIDE 3 - Radiograph of RIGHT ELBOW - Lat.
showing gross enlargement of olecranon and olecranon fossa, together with a large haemophilic cyst.

SLIDE 19 - of another patient showing remarkable similarity to the previous case.

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MATERIALS AND METHODS

Of the six patients selected, 2 were placed on a high potency purified commercial concentrate.
3 were placed on an intermediate commercial concentrate.
1 patient was put on Cryoprecipitate.

DOSAGE

Initially we had decided to raise the patients' Factor VIII to 30% of normal, every other day. However, to avoid wastage of materials and because of the different weights of the patients, the following dosage schedule was adopted.

Patient Initials	Material	Dosage u/Kg	Av.normal mean F.VIII Level
GRO-A	Kryobulin	18.5	30% 66
	Kryobulin	16.2	25% 94
	Cryoprecipitate	(18-29 u/Kg)	37% 89
	Hemofil	12.6	19% 80
	Kryobulin	12.1	22% 96
	Hemofil	9.6+	(11%/20%)

SLIDE

Each patient was trained to prepare the Factor VIII material and inject himself. In addition, the patients kept records of all transfusions in a Home Treatment File.

RESULTS

Initials	Days Observed	Bleeding Frequency/100 days Off	On	% Reduction
GRO-A	229	31.3	10.0	68%
	220	16.6	0.9	94.6%
	219	17.0	1.8	89.4%
	217	16.0	3.2	80%
	190	15.6	0.5	96.8%
	219	14.3	12.	16.0%

NOTE: Bleeding Frequency/100 Days.

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As can be seen from these results, with the exception of the last patient there has been a considerable reduction in the number of spontaneous bleeding episodes. No attempt was made to differentiate between spontaneous and traumatic haemorrhage.

I do not know the reason for the failure of this regime in GRO-A He is on a highly purified concentrate and for the final term of this study he will be switched to N.H.S. concentrate or an intermediate type of commercial preparation.

A normal ½ life for infused Factor VIII has been shown on this patient. Because of the quantity and frequency of transfusion, we were concerned about the possible commulative effects of fibrinogen.

The next slide shows the pre-transfusion fibrinogen levels over a one month period. As one would expect, the highest levels are found in those patients on Kryobulin and Cryoprecipitate and the lowest levels on Hemofil.

There is no significant difference between the levels and all are within the normal range.

Pre Transfusion Fibrinogen Levels over 1 month

Initials	Material	Start	End
GRO-A	Kryobulin	315	315
	Hemofil	200	200
	Kryobulin	260	260
	Hemofil	192	180
	Kryobulin	285	250
	Cryoprecipitate	305	300

RADIOLOGY

Two of the patients have shown improvement.

GRO-A - Improvement of appearances of LEFT KNEE.
- Improvement of RIGHT KNEE. Appearances are virtually normal.

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The two patients who showed the greatest improvement in bleeding frequency have also improved radiologically.

In one case GRO-A the X-Rays of the RIGHT KNEE are virtually normal. In the other GRO-A, the LEFT KNEE has improved.

However, those joints which have sub articular cysts, have shown no improvement and in two of the patients GRO-A and GRO-A, there has been considerable enlargement of the cysts.

Clinically with the exception of GRO-A all the patients have shown a marked improvement in their joint function and increase in power of those muscles which affect the damaged joints.

Frequent testing for inhibitors on all patients were uniformly negative. No cases of hepatitis have occurred throughout the observed period.

COSTS

Prophylaxis of this type is expensive. The following table shows the cost/day of therapeutic materials OVER and ABOVE that required for on demand treatment of bleeding episodes.

GRO-A	£4.00 per day
	£18.4 per day
	Cryoprecipitate estimate not possible
	£15.2 per day
	£13.2 per day
	£12.8 per day

CONCLUSIONS

Two types of patients would appear to benefit most from prophylaxis.

1. The most severe haemophiliacs with bleeding frequencies of the order of GRO-A This I would imagine is a very small number and the cost of such a regime is relatively small. GRO-A was on a high dosage regime viz 18.5 u/Kg and by reducing his prophylactic dose by 100 units per transfusion his on demand use of material would balance that used in prophylaxis.

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2. Those patients with one affected joint for whom short term prophylaxis would seem to be appropriate.

We are not able to explain the failure of prophylaxis in the last patient, GRO-A This may be related to the product and during the next term he will be placed on an intermediate type of concentrate.

Frequent post transfusion and inhibitor assays were performed and at no time was there evidence of the development of Factor VIII antibodies. In addition, in vivo ½ life studies were normal.

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