Haemophilia Home Therapy

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To Dr Tom Boon, lately physician to the Royal Victoria Infirmary, and first Director of the Newcastle Haemophilia Centre

2. SEVERE KNOCKS TO THE HEAD OR SEVERE OR PERSISTENT HEADACHE (see also page 75).
3. SEVERE OR RAPID SWELLING IN ANY SITE.
4. SEVERE PAIN IN THE CHEST OR ABDOMEN.
5. VOMITING, OR COUGHING UP OF BLOOD, OR PASSAGE OF BLOOD IN THE STOOL OR URINE.
6. OPEN WOUNDS REQUIRING STITCHES.

WHEN IN DOUBT – CONTACT YOUR CENTRE.

There will occasionally be times when you will want to try and *prevent* a bleed – for instance before an important examination, interview or social event. Your Haemophilia Centre doctor will advise you on the timing and doses of concentrate to give on these occasions.

We are convinced that the single most important aspect of haemophilia care is the speed with which bleeds are treated, and this fact is emphasised several times during training and in the patient's written instructions.

THE RULES AND REASONS FOR HOME THERAPY

1. *THE EARLIER THE BETTER*
Early treatment of a bleed prevents later damage. The more blood that is allowed to enter a joint or muscle the greater the subsequent damage to the tissues, and the longer the time taken for recovery. Early treatment usually allows an immediate return to school or work, and also diminishes the chance of arthritis and disability later in life.
2. *IF IN DOUBT, TREAT*
Trust your, or your child's, 'aura'. If you feel that a bleed might have started, treat it. NEVER wait until a joint is hot, swollen and painful. Do not worry that you may 'waste' the occasional treatment by injecting when a bleed is not present.
3. *A SHOT IN TIME SAVES VIII (or IX)*
In general early treatment saves blood product. A small dose of factor VIII or IX stops small, early bleeds. Bleeds left to develop require more, and often repeated, doses of blood product to stop them.

The recording of treatment is extremely important, and the system in use is discussed in great detail. Patients and their families know and fully understand that only accurate records will ensure further supplies of concentrate. They are taught to appreciate that this rule is in no way a threat, but a means of assuring a patient's continued safety by the early identification of problems, and the prevention of later disability. Every family knows that the use of human blood products carries the

risk of hepatitis. They are aware that this risk has been linked particularly to commercial concentrates prepared from the blood of paid donors, and they know that these risks still exist despite the increased sensitivity of donor tests for hepatitis B.

Families are taught the symptoms and signs of hepatitis, and asked to report to the centre immediately the affected member becomes jaundiced. Explicit instructions on the handling of equipment to eliminate the risk of accidental puncture with contaminated needles ('needle-stick') are given, and due attention paid to the careful disposal of used equipment in order to reduce the risk of hepatitis spread.

Head injury

In the course of the early consultations with patients and their families the importance of the early recognition and treatment of possible intracranial haemorrhage is stressed. This aspect of management is emphasised again during home therapy training, families being taught to contact the haemophilia centre immediately should the patient have an accident involving the head, or develop severe headache, increasing drowsiness, periods of confusion in which he fails to recognise relatives or surroundings, vomiting or weakness or sensory changes in either arm or leg.

As the major cause of death in haemophilia is intracranial haemorrhage it is our routine to admit all patients with a history of significant head injury to hospital for regular replacement therapy and observation. When doubt exists computer assisted tomography is performed in addition to skull radiology.

DAY TWO – PRACTICAL

The first step in the practical training is the teaching of the technique of venepuncture. Almost all of the patients or their parents being trained will have practical experience of all aspects of blood product infusion apart from the actual venepuncture, and this presents no fear to the patient who will have learnt to accept it as a natural part of his life from the age of 2–3 years.

The anatomical sites of easily accessible veins are shown, and simple hints on how to encourage vein filling and stability during injection are given. The veins used most often are those on the dorsum of the hand or in the antecubital fossa. Whilst those on the dorsum of the hand appear particularly appropriate when another person is giving treatment it is the veins of the antecubital fossa that find most favour with our patients. Self-infusion is also commonly practised at this site, not

or, when the household does not have acces[illegible]an open fire, returned to the centre in sealed polythene bags. In Newcastle these bags, labelled 'Biohazard: hepatitis risk' are issued as standard practice with all replacement stocks of concentrate and venepuncture equipment.

Hepatitis warnings

However carefully one tries to regulate the use and disposal of potentially hazardous equipment mistakes will be made, and families should know what to do when they occur.

Parents involved in a home therapy programme should teach their children that syringes are dangerous and are not play-things for use as water pistols. Families should be told that ordinary washing of materials contaminated with blood or blood product does not remove the hepatitis virus, and that if any blood, cryoprecipitate or concentrate is spilt the area should be wiped clean with domestic bleach.

In the event of needle-stick by someone other than the haemophiliac the incident should be reported to the centre or the family doctor immediately. Five cases of someone else inadvertently pricking themselves with a used needle have been reported to the Newcastle centre since 1973, three of these involving hospital staff. Local procedure is to administer specific immunoglobulin to the victims. In one case the parent of a severely affected haemophilic boy became HB_sAg positive, without clinical jaundice, after the accident.

8 Veins and vein care

The veins are the haemophiliac's lifeline. They should not be assaulted by the inexperienced student learning venepuncture, by the houseman in a hurry to reach the next emergency or by the doctor intent on using the most sophisticated (and expensive) cannulae for the short-term infusion of clotting factor. They should never be subject to cut-down (surgical exposure), which will render them useless thereafter, except in the most dire emergency. The repeated venepunctures of haemophilic management require calm, patience, experience based on sound teaching and technically good small-vein sets, preferably of the winged Butterfly type. Satisfactory oral clotting factor therapy (Hemker and colleagues, 1980) is unlikely to supersede intravenous treatment for some years, and even if it proves practical, is probably not going to provide high enough *in vivo* recovery levels for the management of major haemorrhage or surgery.

Local complications of venepuncture and intravenous therapy seen in hospital include bruising, erythema and oedema, phlebitis and thrombophlebitis. All are more common when technique is hurried or imperfect, when devices of large calibre or length are used in preference to small-vein sets, and when devices are left *in situ* for long periods of time. In over 15 000 blood product infusions by patients on home therapy (or by their parents) using small-vein sets the only local complications we have seen have been transient erythema along the course of the vein with some intermediate potency blood products and the very occasional tender, thrombosed vein. There have been no serious systemic complications such as septicaemia, catheter embolism or air embolism.

CHOICE OF VEIN

Despite the ease and lack of pain of self-venepuncture when using the veins on the dorsum of the hand the majority of our patients prefer to

with diluent according to the manufacturers' instructions. Mixing was manual, the study mimicking home rather than hospital preparation. A minimum of three vials of each product was subjected to each test.

Differences between the products were evident, those of note being:

(1) solubility (the time taken from completion of the addition of diluent to the disappearance of all solid matter into solution) ranged from 2 minutes 53 seconds with Hemofil (Travenol) to 47 minutes 35 seconds with Kabi;
(2) particle counts on reconstituted material, performed on a Coulter channeliser C1000, revealed 3 groupings of products: the Abbott material, Profilate, contained $> 46 \times 10^4$ particles/0.1 ml; NHS Edinburgh AHG, Factorate (Armour) and Humafac (Parke Davis) $23-26 \times 10^4$ particles/0.1 ml, and the remainder $4-7 \times 10^4$ particles/0.1 ml.
(3) total protein content varied, Humafac containing significantly more protein than the other products, with the exception of Elstree. Correlation of protein with VIII:C removed this significance, however;
(4) fibrinogen content was high (in excess of 10 g/ml) in NHS Edinburgh AHG, NHS Elstree AHG, Humafac, Kabi and Profilate, and low (< 1 g/100 ml) in the remaining products. In no case did fibrin degradation products exceed 10 μg/ml;
(5) immunoglobulin content varied, Humafac containing significantly more IgG than the other products, and Kabi significantly less IgG. Humafac also contained more IgA and IgM;
(6) the majority of products contained < 2 mg/100 ml of antithrombin III, the exceptions being Humafac (mean 16.2 mg/100 ml), Kryobulin:Immuno (mean 4.6 mg/100 ml), and NHS Edinburgh AHG (mean 4.2 mg/100 ml);
(7) at least one sample of NHS Edinburgh AHG, Factorate:Armour, and Humafac and the three samples of Koate:Cutter tested had anti-A isohaemagglutinin titres of 1 in 64. Anti-B titres were also 1 in 64 in the Koate samples.

We were pleased to find that comparison of initial VIII:C measurements with manufacturers' statements of vial content showed no significant discrepancies, and there were no differences in stability at 37 °C among the products. Most products contained about four times as much VIIIR:Ag as VIII:C. Bacteriological analyses at zero and after 48 hours' incubation were consistently negative.

Our conclusions from this study, reported more fully in the proceedings of a workshop on the management of the haemophilias (Jones and

his colleagues, 1980) were that, through failures in definition and communication between manufacturers and doctors, clinicians were often unaware of what they were injecting into their patients in addition to factor VIII:C and sterile water, and that this paucity of knowledge was not in the best interests of their patients. Since this study new products have been introduced to the market, or are presently undergoing clinical trial. They include a high purity concentrate (HP Factorate, Armour), an intermediate purity form of Hemofil (Travenol), and a product developed from porcine blood by Speywood Laboratories. Although the latter does not have the thrombocytopenic effect associated with first generation animal products, it is too early to comment on its long-term efficacy in the individual patient. Work has continued on methods of preparing low fibrinogen and total protein concentrates of factor VIII without a corresponding loss of yield, and on the possibility of manufacturing 'synthetic' products by the genetic manipulation of cell or bacterial cultures. Despite the fact that this work is in its infancy it is especially important because it holds the promise of producing therapeutic materials free of all forms of hepatitis, and it is the transmission of the various viruses of hepatitis which appears to present the greatest threat to the health of the haemophiliac without high titre antibodies (Editorial, 1975). In the present state of our knowledge there is no way to remove this threat, apart from rigorous testing for hepatitis B, because it is probable that changes in liver function and architecture reflect challenge by more than one 'non A, non B' viral agent.

It has been suggested that large pool factor VIII concentrates should not be prescribed for children, who should receive only cryoprecipitate (McGrath and colleagues, 1980), but such an approach is impractical if severely affected children are to benefit from the early cessation of haemorrhage which home therapy affords, and it begs the question of exactly when to introduce concentrates. There is evidence that no long-term difference accrues anyway, Levine and his colleagues (1977) demonstrating that abnormalities in liver function were as prevalent in haemophiliacs treated only with cryoprecipitate prepared from voluntary donor plasma as in those who had been subjected to multiple transfusions with commercially prepared concentrates. In addition, it is difficult to understand why the reported histopathological features of liver disease do not seem to be reflected in an increased morbidity or mortality even in those populations of haemophiliacs subjected to very high doses of large pool preparations for many years. McGrath and his colleagues reported that the biopsies performed on four of five haemophilic boys with persistently abnormal liver function tests showed the changes of chronic persistent hepatitis, a disorder associated with a

lived 25 miles from the haemophilia centre, and this charge would not include the cost of blood product. The mean number of bleeds treated at home by patients on our programme was 33 in 1978.

On these simple calculations alone it can be argued that home therapy represents a saving to the state. Ingram and his colleagues (1979), considering other aspects of the economic advantages to the family on home therapy, reached the same conclusion, and emphasised the effect of keeping the haemophilic breadwinner in employment. In the United Kingdom the average annual wage for a normal worker in 1979 was about £4000. The man on home therapy and in employment would, in addition to being able to provide this sum for his family, have saved the state £2800 in unemployment and sickness benefit.

Haemophilia home therapy costs compare favourably with those of home based renal dialysis (about £4000 in 1979). Both the patient with severe haemophilia A and the patient in chronic renal failure cost the state considerably less than the incarcerated juvenile delinquent, about £5000 per year in 1979 (Jones, 1980b).

FOLLOW-UP AND RECORDS

A template for recording the progress of individuals with haemophilia

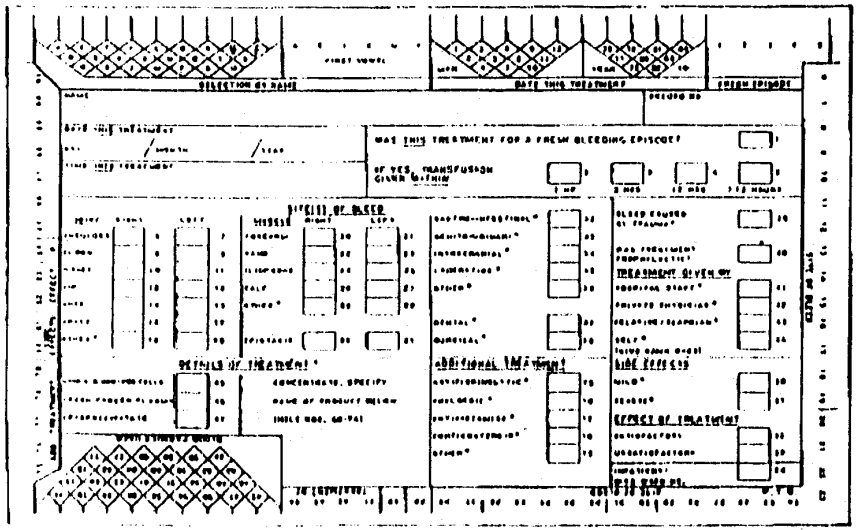
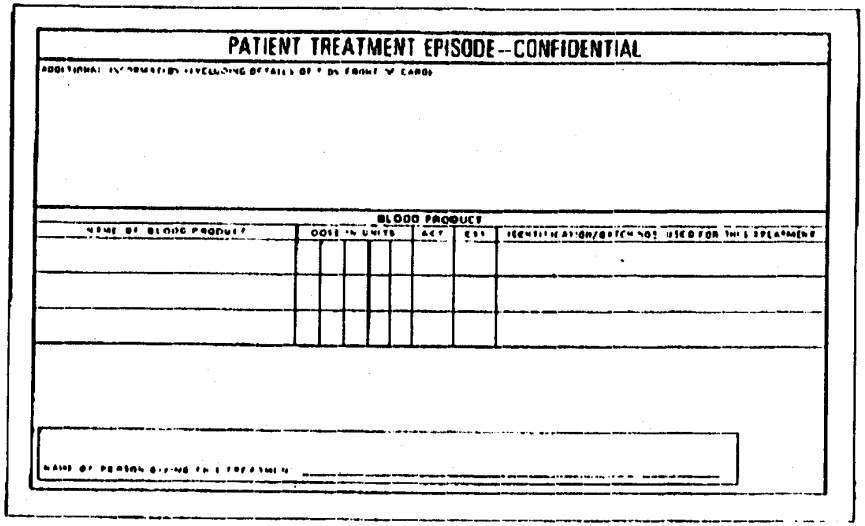


Figure 13.2(a)



(b) Figure 13.2 (a) and (b) Haemophilia record card: (a) front, (b) back

has been described in the World Federation of Haemophilia Booklet *Haemophilia Medical Records and Data Collection* (1979), from which Figures 13.2–13.4 are taken.

Whether or not a patient is on home therapy it is suggested that certain facts must be known about this progress in order that appropriate treatment can be prescribed. In summary the facts which should be ascertained for a given period of time are:

(1) the total number of bleeds;
(2) the number of bleeds that were spontaneous;
(3) the number of bleeds caused by trauma;
(4) the sites of bleeding;
(5) the timing of treatment;
(6) who gave the treatment;
(7) the type of blood product used;
(8) the dose of treatment;
(9) whether treatment had to be repeated;
(10) whether there were any side-effects.

Details of the blood product used should include the reference numbers of the batch or lot numbers for retrospective analysis in case of hepatitis, or other possible side-effects of therapy.