brings into sharp focus the lethal character of this disease. It is important to stress the fact that five of the 14 patients were completely asymptomatic. An inescapable inference from this report is that drug abuse may be a factor in necrotizing angiitis.

We are indebted to John C. Norris, M.D., for assistance.

References

1. Zeek PM: Periarteritis nodosa and other forms of necrotizing angiitis. New Eng J Med 248:764-772, 1953
2. McCombs RP: Systemic "allergic" vasculitis: clinical and pathological relationships. JAMA 194:1059-1064, 1965

HOME TRANSFUSION FOR PATIENTS WITH HEMOPHILIA A*

S. Frederick Rabiner, M.D., and Margaret C. Telfer, M.D.

Abstract A program was established to train relatives of hemophiliac patients deficient in antihemophilic factor to administer concentrate of the factor intravenously at home after telephone consultation with the physician. Eighteen months' experience with the program indicates that with careful medical supervision, home transfusion is practical and safe. Consumption of antihemophilic-factor concentrate is increased, probably because of greater willingness to report hemorrhages. The number of school or work days lost is decreased on the program, but it is too early to estimate lower morbidity in terms of permanent joint damage. Patients and their relatives are enthusiastic because of the time saved, rapid relief of pain and opportunity of helping the patient within the family unit. Until prophylactic therapy becomes feasible, home transfusion is a reasonable substitute.

THE life of the patient with hemophilia is made difficult by a host of problems, of which two are paramount: the constant possibility of a disabling or life-threatening hemorrhage and the paucity of medical facilities manned by personnel trained and willing to treat hemophilia. Although the development of cryoprecipitate[1] and other antihemophilic-factor (AHF) concentrates[2,3] has facilitated and extended treatment of hemophilia these problems still exist. Even though prophylactic therapy is at present impractical, it is possible, by prompt AHF replacement therapy for each episode of bleeding, to reduce greatly the duration of disability and long-term crippling effects of joint hemorrhages. To accomplish this, patients must be taken by their family or friends (frequently at night) to a medical center, wait to be seen by a physician, wait for reconstitution of the AHF preparation, receive AHF replacement therapy and return home. The interval between onset of hemorrhage and institution of therapy depends on travel time, patient load in the clinic or emergency room and efficiency of the hospital staff. These factors frequently result in a delay of several hours.

The hemophilia clinic of Michael Reese Hospital serves a group of 86 patients with hemophilia spread over a 150-mile radius. An additional 20 to 30 are seen periodically in consultation for special problems. Although Chicago has an excellent highway system, the necessity of traveling long distances with a bleeding patient, frequently through congested traffic, presents a real problem.

On several occasions we asked local physicians to share the responsibility for care of patients with hemophilia with us. This was rarely successful because physicians in small communities see very few such patients and have great difficulty maintaining the necessary 24-hour emergency service. In addition, many physicians do not appreciate the necessity for prompt replacement therapy, and some even withhold treatment for a variety of fallacious or outmoded reasons. Nevertheless, the patients and their families know the value of adequate therapy and will go to any lengths to get it.

One solution was suggested to us from the experiences of a family with two hemophilic boys who had to move from a community, where the boys received good care, to an area with no hemophilia center. After many frustrations they consulted their previous physician and described their plight. He taught the parents to transfuse their children with fresh-frozen plasma at home, and arranged to keep them supplied with sufficient plasma. When the family moved to Chicago, they joined the Michael Reese Hospital Clinic but continued home transfusion because of its many advantages. They finally told us their story, with great trepidation, fearing that we would ask them to discontinue what had become a way of life to them.

Our initial negative response to this idea quickly gave way to cautious appraisal. We carefully considered the serious problems that might occur during home transfusion of cryoprecipitate. Our experience, and that cited in the literature, has not included any case of anaphylaxis. The most frequent reaction consisted of hives and itching, which usually responded quickly to diphenhydramine hydrochloride. The use of sterile disposable plastic needles and filters, as well as training in aseptic technic, would essentially eliminate the possibility of infection. The technic of venipuncture itself was simple and

*From the Division of Clinical Hematology, Department of Medicine, Michael Reese Hospital and Medical Center, Chicago (address reprint requests to Dr. Rabiner at the Division of Clinical Hematology, Michael Reese Hospital and Medical Center, 29th St. and Ellis Ave., Chicago, Ill. 60616).

presented no serious problem. The major obstruction to home transfusion were medicolegal considerations concerning the responsibility, usually reserved to licensed physicians, of intravenous administration of blood products. Our legal consultant believed that the precedent of experimental programs, such as home dialysis units for renal disease, permitted delegating such responsibility, under controlled conditions, to paramedical and nonmedical personnel. It was thought that an experimental program for home transfusion might be set up if certain conditions were met. These were as follows: benefit to the patient was anticipated; the patient and his family were clearly informed of any risk involved; the transfusionist was shown to have the ability to prepare correctly and administer the medication intravenously; a physician must approve of each transfusion by telephone and perform careful follow-up examination; and the physician must have full control of blood products issued to the patients.

A home transfusion program, satisfying these criteria, was established. We now report our experience after the first 18 months of its operation.

Home Transfusion Program

The proposed home transfusion program was presented to a general meeting of the Midwest Chapter of the National Hemophilia Foundation, after approval of the chapter's medical advisory committee. Volunteers for the program were requested. Sixteen families comprising 18 patients were selected mainly on the basis of a self-reliant, even-tempered member who would serve as transfusionist. Since only cryoprecipitate was used initially, patients with hemophilia B were not chosen. Transfusionists were assigned to classes of three to four persons, where they were taught to prepare the AHF preparation, to draw it up into syringes and finally to inject from these syringes intravenously through a 23-gauge scalp-vein set. When cryoprecipitate was used it was drawn through a filter into syringes. Filters, syringes and scalp-vein sets were disposable and therefore used once and discarded. Before graduation the student had to transfuse the patient four or five times in the clinic successfully, under observation. After this, the family was given a supply of AHF for home transfusion. Cryoprecipitate was transported in styrofoam baskets with dry ice and stored at −39°C in home freezers. Concentrate was transported in ice and stored in a refrigerator.

With each suspected hemorrhage the transfusionist consults the hematology resident on duty by telephone. The physician then determines whether or not therapy is indicated and if the patient should be taken to the hospital for examination or given a transfusion at home. If home transfusion is indicated the resident determines the dose, gives instructions for supportive measures such as immobilization and analgesics, and directs the family to telephone the next day to report progress. Since the clinic serves as the sole source of supply of AHF, and since we know how much is authorized by telephone, we are able to enforce physician consultation before transfusion.

Our usual recommended dose for joint or soft-tissue hemorrhage is 10 to 20 U per kilogram of body weight. This is determined by the location and severity of hemorrhage. The calculated amount is rounded off to accommodate the number of units per bag of cryoprecipitate or vial of concentrate. If there is any doubt of the severity of hemorrhage the patient is instructed to report to the hospital for examination. All patients suspected of having gastrointestinal or other potentially life-threatening hemorrhages are seen in the hospital and admitted if necessary. Under these circumstances, we frequently direct the family to give AHF before leaving home.

In 16 families trained for the program, three patients have become inactive because their hemorrhages are so infrequent that they would rather report to the clinic for treatment. These patients are two adults and one child. Another family was initially unsuccessful because the child refused to allow his parents to perform venipuncture. This eight-year-old boy had many emotional problems, which have responded to psychiatric treatment. He is now transfused at home by his mother.

The other 12 families, consisting of 14 patients, have remained in the program (Table 1). None of these patients had mild (AHF over 5 per cent) hemophilia. AHF assays were performed by a modification of the methods of Rapaport et al.,[4] as previously described.[5] Eight cases were severe (AHF 0 to 2 per cent), and six moderate (AHF less than 5 per cent, but over 2 per cent). The patients on the program ranged in age from two to 39 years. The youngest was eight months old when his mother started to treat him. The member of the family who most frequently performs the infusion is the mother. One adult with hemophilia is given infu-

Table 1. Data in 14 Patients in 12 Families.

Patient	Age (Yr)	Degree of Hemophilia	Person Giving Infusions	Distance to Hospital (Miles)	Travel Time to Hospital (Min)
G. K.	13	Moderate	Mother	45	60
B. B.	6	Severe	Mother	25	60
W. M.	15	Severe	Mother	22	60
J. M.	20	Moderate	Mother	30	45
R. R.	12	Severe	Mother	5	30
T. T.*	11	Moderate	Mother	65	60
C. T.*	15	Moderate	Mother	65	60
G. R.	16	Severe	Mother	20	45
J. S.	30	Severe	Wife	25	60
H. K.	10	Moderate	Mother	12	35
J. I.	39	Moderate	Patient himself	18	40
R. T.*	5	Severe	Mother	135	180
S. T.*	2	Severe	Mother	135	180
G. R.	16	Severe	Mother	135	180

*Brothers.

sions by his wife, and another either by his brother or by himself. These families live some distance from the hospital. Although it takes the closest family 30 minutes to reach the hospital it takes 2½ hours for a family with two hemophilic boys, who live 135 miles from the hospital.

The families were asked to fill out a questionnaire describing their experience with the home transfusion program (Table 2). At the time of this evaluation, nine of the patients have been on the program for 18 months, one for one year, and four for six months. They were asked to grade emotional reactions of transfusionist and patient on a 4+ (strongly positive) to 4− (strongly negative) scale both initially and at present. In addition, problems in venipuncture, dissolving cryoprecipitate, filling syringes and so forth were graded from 0 to 4+.

Table 2. 18-Month Evaluation by Participants.

Evaluation of Program		No. of Responses*								
		−4	−3	−2	−1	0	+1	+2	+3	+4
Aceptance of home transfusion concept:										
Patient	Initial	1	0	0	1		1	1	3	7
	Present	0	0	0	0		1	0	4	9
Transfusionist	Initial	0	0	0	0		1	2	5	6
	Present	0	0	0	0		0	1	2	11
Emotional reaction to home transfusion:										
Patient	Initial	1	0	0	2		1	1	4	5
	Present	0	0	0	0		1	1	3	9
Transfusionist	Initial	0	0	1	0		2	3	6	2
	Present	0	0	0	0		0	1	2	11
Technical difficulties with transfusion:										
Venipuncture	Initial					2	11	0	1	0
	Present					7	7	0	0	0
Filling syringe	Initial					9	5	0	0	0
	Present					11	3	0	0	0
Dissolving concentrate	Initial					9	4	0	1	0
	Present					12	0	0	2	0

*See text for grading of response.

There was general acceptance of the program by the mothers initially, and in all cases they are now even more satisfied with the system. Although the younger patients had particularly negative emotional reactions at the onset, they now universally prefer the program to treatment at the clinic. All reported some difficulties initially with venipuncture and dissolving AHF concentrates, but all consider this to be no longer a problem.

During this period the patients received a total of 317 injections of AHF preparations, all but 26 of which were performed at home. The reasons for the 26 clinic visits were as follows: six patients had exhausted their supplies of concentrate; two had venipuncture problems; and 18 visits were due to uncertainty on the part of the doctor or the patient about the extent of the bleeding.

There were no severe reactions after home infusion to AHF. Four patients described one to two episodes of hives and itching, which responded quickly to oral diphenhydramine hydrochloride. None required hospitalization.

An investigation was made of the number of days the patient missed from school or work before and after institution of home transfusion. An effort to obtain data for this comparison from school or job records was made by the families. This information was available for eight patients (Table 3). When statistically analyzed, with a paired t test, the data revealed a significant (p less than 0.05) decrease in days absent on home transfusion in four patients, and no difference in the others.

We examined our clinic records for changes in frequency of hospital admissions, number of hemorrhages, amount of AHF used and number of repeat visits for the same episode (Table 4). Although there was no significant change in the number of hospitalizations or hemorrhages, there was a significant (p less than 0.05) increase in the number of AHF units infused. Repeat visits with bleeding were not more necessary after than before the home transfusion program.

In closing the questionnaire, we asked the families for spontaneous comments about the program. All reported a great saving of time, particularly at night, when the emergency-room wait had been the longest. Two families reported much decreased consumption of analgesics, and two verified a greater willingness of the child to report hemorrhages. Three found that they saved money on repeated

Table 3. Days Absent from Work or School per Month during the Study as Compared with the Same Period in the Preceding Year.

Patient		Days Absent*	No. of Mo
J.S.	On study	0.6 ± 0.5	7
	Yr before	2.1 ± 1.3	7
J.I.	On study	0.6 ± 1.0	11
	Yr before	1.8 ± 2.7	11
H.K.	On study	1.7 ± 1.9	6
	Yr before	2.8 ± 2.3	6
T.T.	On study	5.7 ± 3.5	9
	Yr before	7.2 ± 3.8	9
C.T.	On study	1.8 ± 0.9	8
	Yr before	8.7 ± 5.1	8
G.R.	On study	0.0 ± 0.0	5
	Yr before	0.8 ± 0.4	5
B.B.	On study	3.5 ± 2.6	9
	Yr before	3.0 ± 2.5	9
W.M.	On study	0.7 ± 0.5	4
	Yr before	1.0 ± 1.2	4

*Mean ± S.D.

Table 4. Changes in Hospital Admissions, Hemorrhages and AHF Units Given.

Patient	Time on Study (Mo)	No. of Admissions		No. of Hemorrhages		Approximate No. of AHF U Infused		
		A*	B†	A	B	A		B
						clinic	*home*	
J. S.	6	0	0	2	3	0	240	3,300
J. I.	18	1	0	10	11	9,000	4,500	7,800
H. K.‡	12	0	1	18	19	0	15,000	3,000
S. T.‡	16	1	—	10	—	600	6,210	—
R. T.‡	18	1	6	27	20	1,800	6,240	6,000
R. R.	6	0	0	6	3	900	3,000	1,500
G. K.	18	0	0	29	3	600	18,240	2,700
T. T.‡	19	0	4	43	16	0	31,600	6,000
C. T.‡	19	0	3	17	16	0	10,500	5,800
G. R.	6	1	0	5	9	900	2,100	6,300
J. M.	15	0	0	7	0	0	6,600	3,300
B. B.	18	0	1	15	14	1,500	3,900	3,900
W. M.	6	0	1	2	3	600	600	2,100
G. R.	18	3	1	13	17	3,600	3,300	4,500

*At time of study †At equivalent time before study. ‡Brothers.

emergency-room visits and car costs, although the increased amount of concentrate somewhat lessened this saving. One commented that the patient's siblings benefited since they were not as frequently left with a baby sitter at night. There were no complaints or report of any mishaps, although such comments were requested.

Discussion

From the experience with the home transfusions at Michael Reese Hospital and Medical Center a program of venous infusion of AHF preparations by members of the hemophiliac patient's family, under a doctor's supervision, appears feasible and practical. We have found that the patients and their families are universally enthusiastic about the plan and that they believe their hemorrhages are treated faster, their pain stopped sooner, and their lives are less disturbed by the disease than at any time in the past.

We have found that hemorrhages are clearly described by patients and relatives and that potentially life-threatening situations are recognized and the patient taken to the hospital. Our physician group is cautious and requires a visit to the clinic for any hemorrhage of whose extent they are uncertain. This necessitated only 16 visits out of 317 episodes of hemorrhage. The majority of hemorrhages, which occur in joints or soft tissues of the extremities, can be safely treated at home. We have had no serious allergic manifestations to the AHF preparations employed.

However, the approval of the patient and the lack, so far, of serious mishaps are not sufficient to recommend such a program. We must show benefit to the patient that outweighs the small risk of having an intravenous infusion of protein material performed at some distance from a physician. A theoretical long-term effect of home transfusion is based on the clinical impression that prompt treatment of joint hemorrhages would reduce trauma and delay onset of chronic arthropathy. The period covered by the study is too short to expect objective changes, but there is no doubt that home transfusion shortens the length of time between onset of hemorrhage and AHF infusion. In addition immobilization can more easily be accomplished since the patient does not have to be transported to and from the hospital. An immediate beneficial effect of home transfusion was the significant reduction in number of days lost from school or work in 50 per cent of patients on whom those data were available.

The cost, to the family, of 1 U of AHF is the same whether it is given in the hospital or at home. Care for hemophilia, in Illinois, is not covered by Crippled Children's Service or any other agency. With home transfusion, there are no emergency-room fees.

One might anticipate that consumption of AHF would be decreased by home transfusion since hemorrhages would be treated sooner. Not only did this not prove to be the case, but there was a significant increase in use of AHF. Some of this increase was due to the fact that the patients were growing, and physicians were using more AHF concentrate. We examined the records of 10 boys treated only in the clinic and found that during these years, they also had an increase in AHF infusion.

However, in our opinion the most important factor responsible for the tremendous rise in the use of AHF is the increase in number of reported hemorrhages. This is borne out by our clinic records, which indicate that before home transfusion, many of the younger boys used to be brought to clinic after two or three days of pain. The mothers believe that the boys are less reluctant to report hemorrhages since they no longer anticipate a trip to the hospital. Thus, we are probably now treating some small hemorrhages that, in past years, would have

subsided without transfusion. Since most of these occur in joints this therapy is, for the most part, indicated.

After 18 months of the home transfusion program we have advanced from cautious appraisal to cautious approval. We have successfully resisted being carried away by our enthusiastic patients, who have spread the word to the other families in the clinic. It must be emphasized that the constant availability of medical supervision and advice by telephone, the strict supervision of the quality and handling of each unit of AHF concentrate, and the continued necessity of a checkup in the clinic are essential to the mechanics of the program. We hope to be able to show, with time, decreased morbidity from repeated joint hemorrhages. We believe that the advantages of home therapy outweigh the theoretical risks, and it is therefore the closest approximation to prophylactic therapy that is now feasible financially.

We are indebted to Dr. Zinet Currimbhoy for instruction of the classes for transfusionists and to Mrs. Rae Williams for technical assistance.

References

1. Pool JG, Shannon AE: Production of high-potency concentrates of antihemophilic globulin in closed-bag system: assay in vitro and in vivo. New Eng J Med 273:1443-1447, 1965
2. Abildgaard CF, Simone JV, Corrigan JJ, et al: Treatment of hemophilia with glycine-precipitated factor VIII. New Eng J Med 275: 471-475, 1966
3. Brinkhous KM, Shanbrom E, Webster WP, et al: A high potency glycine-precipitated antihemophilic factor concentrate: use in hemophilia and hemophilia with inhibitors. Blood 30:855, 1967
4. Rapaport SI, Schiffman S, Patch MJ, et al: A simple, specific one-stage assay for plasma thromboplastin antecedent activity. J Lab Clin Med 57:771-780, 1961
5. Rabiner SF, Friedman LH: The role of intravascular haemolysis and the reticulo-endothelial system in the production of a hypercoagulable state. Brit J Haemat 14:105-118, 1968

PSYCHIATRIC COMPLICATIONS OF OPEN-HEART SURGERY*

A Re-examination

Stanley S. Heller, M.D., Kenneth A. Frank, Ph.D., James R. Malm, M.D., Frederick O. Bowman, Jr., M.D., Paul D. Harris, M.D., Maurice H. Charlton, M.D., and Donald S. Kornfeld, M.D.

Abstract Clinical observation suggested that the prevalence and severity of postcardiotomy delirium had declined in recent years. It was reasoned that a comparative analysis of a current with an earlier sample would document this decline and perhaps shed further light on the etiology of the delirium.

In 67 per cent mental status remained clear. The frequency of delirium preceded by a lucid postoperative interval declined from 38 per cent in 1965 to 24 per cent in 1969. In 9 per cent there was an immediate organic brain syndrome. The following factors, evidently associated with brain dysfunction, were found to be related to the occurrence of delirium: advanced age, severity of preoperative and postoperative illness and time on cardiopulmonary bypass. The postoperative lucid interval suggested that recovery-room factors were also involved. Decreased time required on cardiopulmonary bypass appears to be a primary factor in the reduction of frequency. Modifications in the environment of the recovery room after open-heart surgery may also have contributed to the decline.

IN 1965 a series of reports[1-3] described the frequent occurrence (38 to 70 per cent) of delirium after open-heart surgery. The phenomenon usually followed a lucid interval of two to four days after surgery, while the patient was still in the open-heart recovery room (OHRR). Typically, the patient first experienced a perceptual distortion, such as a floating sensation, and some mild disorientation, progressing in many cases to vivid hallucinations, paranoid delusions and gross disorientation. This "post-cardiotomy delirium"[2] usually cleared within 24 to 48 hours after transfer out of the OHRR.

Recent studies of open-heart surgery[4-10] indicate a reduced frequency of the delirium (10 to 45 per cent). Our clinical impression was also that the prevalence and seriousness of the delirium had diminished. We decided that a comparison with our earlier data[3] could shed further light on the etiology of the phenomenon.

*From the departments of Psychiatry, Surgery and Neurology, Columbia University College of Physicians and Surgeons (address reprint requests to Dr. Heller at 630 W. 168th St., New York, N.Y. 10032).

Supported by a grant (MH-12756) from the National Institute of Mental Health and by a general-research support grant from the U. S. Public Health Service to the Columbia University College of Physicians and Surgeons.

Methods

One hundred patients were selected at random from the adult operative schedule, between 1967 and 1969. All were over 21 years of age except five with congenital heart disease, 18 to 21 years old, included to augment the congenital group. Participation in the study was on a voluntary basis. Eleven patients declined to participate.

Preoperative Evaluation

Preoperative data were collected on admission to the hospital during the two days before surgery.